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Evaluation des thérapeutiques endodontiques. Intérêt éventuel d'un matériau bioactif.

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En remerciement d'avoir accepté de diriger ce travail.

Veuillez trouver ici le témoignage de notre profonde reconnaissance et nos remerciements pour votre sympathie.

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- NANTES _

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Sommaire

Introduction

1. Complexité de l'endodontie :

La thérapeutique endodontique consiste à réaliser l'éviction du tissu pulpaire inflammé ou infecté. La cavité endodontique libre de tissu pulpaire pathologique et d'élément pathogène bactérien est ensuite comblée avec un matériau d'obturation hermétique [1, 2]. Le rôle des bactéries présentes au sein des canaux endodontiques dans l'apparition et le développement des lésions périapicales est bien établie [3-5].

La stratégie du traitement endodontique est de prévenir ou d'éliminer l'inflammation des tissus périapicaux, afin que s'exprime leur potentiel réparateur par ostéocémentogenèse.
La clef de voûte de l'endodontie est donc la décontamination de la lumière canalaire [2], le scellement hermétique du réseau canalaire jusqu'à l'apex [6], tout en respectant les structures périapicales.

Néanmoins, le traitement endodontique est un acte difficile en raison de la complexité de l'anatomie de l'endodonte [7-9].

En effet, la richesse des ramifications canalaires va poser le problème de l'instrumentation, du nettoyage et de l'obturation des canaux latéraux et accessoires [10], et ce, malgré les progrès constants réalisés en endodontie par l'apparition de nouvelles techniques et de nouveaux instruments [11]. Par ailleurs, l'appréciation de la limite de l'endodonte va conditionner la réussite à long terme du traitement canalaire. La longueur de travail établie est en fait un statu

quo, puisque la détermination exacte du foramen apical est soumise à une approximation qui veut qu'elle se situe 0,5 à 2mm en deçà de l'apex radiographique. C'est dire à quel point est incertaine la détermination de la limite apicale idéale [12-14].

L'autre problème auquel est confronté l'endodontiste est l'utilisation de matériaux d'obturation, notamment de Gutta Percha et de ciment de scellement, qui présentent une relative toxicité vis à vis des tissus périapicaux [15-17].

Dans le cas de sur-obturation, les matériaux actuels se comportent comme des corps étrangers responsables d'une inflammation chronique qui perdurera d'autant plus que ces matériaux sont peu résorbables [18]. Dans le cas de sous-obturation, le remplissage incomplet du réseau canalaire va laisser des vacuités qui pourront, surtout après formation de lésions périapicales, contenir des éléments pathogènes (toxines, bactéries). Ces éléments pathogènes y trouveront un milieu favorable à leur développement et pourront donc entretenir une infection des tissus périapicaux.

2. Données épidémiologiques et résultats concernant l'efficacité de la thérapeutique endodontique :

L'analyse de la littérature concernant le succès des thérapeutiques endodontiques et la qualité des obturations canalaires montre une grande variabilité des résultats rapportés sur le sujet [19, 20].

Le taux de succès des traitements endodontiques varient entre 44 et plus de 90% [21, 22]. Le pourcentage de traitements jugés insatisfaisants (sur évaluation radiographique du niveau

d'obturation et/ou de la condensation) peut atteindre 60 à 70% [23]. Par ailleurs, la prévalence des lésions apicales semblent plus importantes sur dents traitées, notamment celles présentant une obturation canalaire de qualité insuffisante [21, 23-35]. Ces études épidémiologiques ont suggéré que la qualité des traitements canalaires affectait directement le pronostic à long terme des dents traitées [21, 30] et que la perte des dents présentant une obturation endodontique étaient plus fréquentes que pour les autres dents [36].

En France, le rapport de l'ANDEM de 1996 [37] explique la variabilité des résultats des thérapeutiques endodontiques par différents facteurs: la compétence du praticien, la pathologie initiale, la situation et l'anatomie de la dent, les techniques utilisées, les critères de succès retenus et la durée du suivi. Un autre élément de réponse **est la nature même des études** qui ont produit ces résultats. Un grand nombre d'entre-elles sont des enquêtes épidémiologiques descriptives, pour la plupart transversales, ne pouvant mettre en évidence de lien de causalité entre échec thérapeutique et la qualité du traitement. [38-41]. Les études longitudinales et les essais cliniques demeurent peu nombreux à cette période [42-48].
Avec l'émergence de la **médecine fondée sur des preuves** (**Evidence-Based Medicine)** [49]**, l'accent a été mis sur** l'importance d'obtenir des preuves scientifiques valides à partir d' études cliniques systématiques telles que des essais contrôlés randomisés en double aveugle, des méta-analyses, des cohortes de grande taille et éventuellement des études de suivi bien construites [38-40].

Depuis la fin les années 1990, les enquêtes épidémiologiques et notamment les études transversales ont donc fait place à des études cliniques dont la méthodologie et l'analyse statistique sont plus adaptées à l'évaluation des facteurs d'échecs en endodontie [39, 50] telles que : des études longitudinales [51-53], des cohortes rétrospectives [54-62], des cohortes

prospectives [63-73] avec un niveau de preuve scientifique probable (grade B), et des études cliniques contrôlées et randomisées [74-78] ou encore des méta-analyses [20, 79-88] avec un niveau de preuve établie (grade A). Les cohortes sont préconisées dans l'analyse de facteurs pronostiques d'une pathologie avec néanmoins une puissance plus élevée pour les cohortes prospectives.

Des méthodes d'analyse multivariée [34, 52, 54, 56, 58-62, 65-71, 74, 78, 89-93] sont utilisées depuis peu pour évaluer les différents facteurs d'échec en endodontie. Elles ont mis en évidence l'importance d'une pathologie périapicale initiale ainsi qu'un défaut d'herméticité coronaire dans l'échec de la thérapeutique endodontique. La qualité de l'obturation canalaire ne semble donc pas être le facteur pronostic primordial. D'autre part, l' analyse de survie a permis de prouver que les dents traitées endodontiquement ont une survie à long terme moins favorable que celle observée des dents sans traitement endocanalaire, avec un risque de perte pour une molaire traitée endodontiquement 7 fois plus élevé que pour une molaire non traitée [78].

Ces analyses multivariées permettent d'exprimer la force de l'association entre le risque d'échec et une **série de variables**, ici des facteurs de risques. Elles sont de 2 types : la régression logistique et l'analyse de survie. Bien que ces deux méthodes soient proches, l'analyse de survie présente l'avantage de pouvoir étudier le pronostic des thérapeutiques au cours du temps avec des périodes de suivi variables. Depuis moins d'une dizaine d'années, les analyses des facteurs d'échec en endodontie réalisées avec des modèles de survie [52, 54, 56, 57, 59, 61, 62, 76, 78, 88, 92, 94] se multiplient, avec des méthodologies et des temps de suivi variables.

3. Objectifs de travail :

Ce travail a pour objectifs (1°) une **meilleure compréhension des facteurs d'échec** de l'endodontie et (2°) **l'étude de la survie au cours du temps** des dents ayant bénéficiées d'un traitement canalaire au Centre de Soins Dentaires de Nantes**, en fonction de la pathologie initiale**. (3°) Nous avons souhaité **explorer le processus cicatriciel périapical** afin de calculer, selon le délai de suivi, la probabilité d'obtenir la disparition complète d'image apicale.

Cette investigation s'inscrit dans le programme de LIOAD (Laboratoire d'ingénierie Ostéo-Articulaire et Dentaire) pour la mise en place de nouvelles stratégies thérapeutiques grâce aux biomatériaux. Au travers de cette analyse, nous voulions identifier les facteurs d'échecs des traitements et savoir si nous pouvions améliorer leur pronostic à long terme, afin d'éviter les avulsions dentaires compensées par des prothèses dentaires onéreuses pour la collectivité publique.

4. Apports spécifiques de ce travail :

Analyser des données de survie, c'est s'intéresser à l'apparition d'un évènement au cours du temps : le décès en général. Mais, d'autres évènements comme la réponse à un traitement (réussite/échec) peuvent être étudiés pour des pathologies où le pronostic vital n'est pas engagé. Dans le cadre d'un essai clinique dont le but est d'étudier un évènement tel que le décès ou encore la guérison du patient, ou encore la disparition d'une pathologie, calculer la fréquence de l'évènement étudié peut se révéler insuffisant. Dans certaines pathologies, il peut être

important d'évaluer dans quel délai l'évènement étudié peut se produire. Dans le cas des pathologies périapicales, la réussite du traitement endocanalaire se traduit par une cicatrisation des structures périapicales avec disparition des symptômes et de l'image radiographique de raréfaction osseuse. Ce phénomène de cicatrisation est un processus dynamique qui met plusieurs mois, voire plusieurs années à s'achever. Dans notre cas, l'analyse de survie permet d'expliquer et de prédire le moment où survient cette cicatrisation ou l'échec thérapeutique en fonction de certains facteurs. En effet, les méthodes d'analyse de survie sont **les méthodes de choix dans les études pronostiques** [95, 96] permettant d'associer la fréquence et le **délai** de survenue de l'événement étudié.

La particularité des analyses de survie (par rapport à la régression logistique) est de pouvoir prédire la survie ou la réussite d'une thérapeutique au cours du temps alors que tous les sujets ne sont pas encore guéris ou que l'échec du traitement par exemple ne s'est pas encore produit pour la totalité des patients. Nous avons donc la possibilité d'analyser des résultats **alors que les informations sont partielles (données censurées) et que le temps d'observation ou de suivi varient d'un patient à l'autre.**

Les durées d'observation inégales pour les sujets sont un problème fréquent en recherche clinique, et ceci même lors d'études prospectives bien menées. De plus, la régression logistique qui a été proposée par certains auteurs pour l'analyse multivariée des facteurs d'échecs en endodontie ne peut renseigner sur l'évolution de la proportion d'échec au cours du temps. Le choix d'un modèle de survie comme le modèle de Cox semble donc d'un grand intérêt puisqu'il tient compte des variations de la période de suivi et permet de **calculer la probabilité de succès/échec d'une thérapeutique à différents temps** sur la période d'observation de l'étude.

L'originalité de notre analyse de survie provient également du choix de nos critères d'évaluation. En général, pour les précédentes études réalisées dans ce domaine, l'événement

observé dans le temps est l'échec du traitement endodontique [52, 56, 57, 59, 61, 62, 76, 92]. Or, concernant le traitement des dents avec des lésions périapicales, nous ne sommes pas confrontés à une situation clinique classique du type échec/réussite. Nous pouvons avoir effectivement l'absence de cicatrisation ou la cicatrisation périapicale complète ou subtotale, mais nous rencontrons également des situations intermédiaires, des situations sans évolution de l'image radiographique de la lésion apicales décrites comme cas incertains. Le délai de cicatrisation périapicale semble variable [18, 45, 53, 62, 64, 88, 97, 98]. Bien qu'il soit recommandé de faire un suivi du traitement endodontique au bout d'un an [50, 99], plusieurs auteurs pensent qu'une période de suivi de plusieurs années serait nécessaire pour s'assurer d'une cicatrisation complète [45, 64, 97]. Alors que certains travaux [53, 100] concluent que la majorité des succès et des échecs se produisent lors de la première année, d'autres montrent que la probabilité d'obtenir une **cicatrisation totale** à 12 mois est inférieure à 0.15 [88].

Très peu d'études pronostiques utilisant l'analyse de survie ont exploré les facteurs prédictifs et le délai de survenue de la cicatrisation apicale [57, 88, 95]. Il nous semblait donc intéressant **de prédire dans le temps la régression d'une lésion périapicale préexistante** après traitement endodontique. Pour le groupe de sujets avec une pathologie périapicale initiale (AP+), nous avons donc proposé une première analyse portant sur l'échec (événement classiquement étudié dans la littérature), complétée par une analyse portant sur le succès thérapeutique c'est-à-dire la disparition ou la réduction sub-totale des signes radiographiques de pathologie périapicale.

5. Organisation de notre analyse :

Deux parties constituent ce rapport:

Tout d'abord, une **réflexion sur l'apport des biomatériaux en endodontie**, qui a fait l'objet d'un premier article.

La seconde partie comprend le travail **de recherche clinique avec utilisation d'un modèle de survie multivarié** (modèle de Cox) pour étudier la survie à long terme des traitements endodontiques réalisés selon les bonnes pratiques cliniques [40, 50, 101] au Centre de Soins Dentaires de Nantes.

1) La première étape de cette évaluation clinique est une **étude longitudinale rétrospective** : les patients recrutés ont bénéficiés d'un traitement endocanalaire un an au moins avant leur recrutement.
2) Cette première étude a été complétée par une **étude longitudinale prospective** où les patients ont été identifiés au moment où ils ont été traités. Ils sont suivi jusqu'à leur sortie d'essai ou à l'arrêt de l'étude (Juin 2011).

Cette recherche clinique fait également l'objet de 2 autres articles.

Partie I : Biomatériaux en endodontie.

Prolégomènes :

Nous avons envisagé cette analyse des facteurs pronostiques des traitements endodontiques comme le nécessaire préambule au développement de biomatériaux en endodontie, il a quelques années déjà. A ce moment là, les matériaux dans ce domaine sont rares : seul le MTA® (Mineral trioxyde Agregate) se trouve disponible pour des applications telles que l'apexification, la fermeture des perforations du plancher pulpaire ou de perforations radiculaires, l'obturation rétrograde. Aucun matériau n'est alors proposé comme véritable alternative à l'exérèse de la pulpe ou du tissu nécrotique, dans le traitement des pathologies pulpaires irréversibles et des pathologies périapicales [102].

Par ailleurs, l'influence de la qualité de l'obturation endodontique sur le pronostique des thérapeutiques endodontiques est mis en exergue à partir d'études épidémiologiques publiées, dont une grande majorité d'études transversales [103] ; ce qui relance le débat contradictoire entre l'importance relative de la qualité d'obturation par rapport à l'élimination d'éléments pathogènes et des toxines bactériennes [104]. L'analyse de la littérature en endodontie rapportant des taux de succès très variables [19, 103], plusieurs questions sont apparues : Quel bénéfice peut apporter un biomatériau en endodontie ? Quel est la place d'un matériau bioactif dans le traitement des pathologies pulpaires irréversibles et des pathologies périapicales ?

Quelles qualités faudraient-ils privilégier pour un biomatériau à vocation endodontique : des qualités techniques comme l'injectabilité pour obtenir une obturation du réseau endocanalaire, des qualités biologiques pour induire la formation de tissus minéralisés et favoriser la cicatrisation apicale, ou des qualités antibactériennes pour améliorer la désinfection endocanalaire ?

Il était donc primordial de faire une revue de la littérature des travaux entrepris dans ce domaine, d'en évaluer les résultats et de faire le point sur les différents axes de recherche et de développement des biomatériaux en endodontie.

Partie I: Article

Bioactive materials in endodontics

Paru dans Expert Review of Medical Devices

2008

Bénédicte Castelot-Enkel, Cecile Dupas, Valérie Armengol, Jonas Akpe Adou, Julia Bosco, Guy Daculci, Alain Jean, Olivier Laboux, Racquel Z LeGeros and Pierre Weiss.

Review

EXPERT REVIEWS

Bioactive materials in endodontics

Expert Rev. Med. Devices 5(4), 475–494 (2008)

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Endodontic treatment in dentistry is a delicate procedure and many treatment attempts fail. Despite constant development of new root canal filling techniques, the clinician is confronted with both a complex root canal system and the use of filling materials that are harmful for periapical tissues. This paper evaluates reported studies on biomaterials used in endodontics, including calcium hydroxide, mineral trioxide aggregate, calcium phosphate ceramics and calcium phosphate cements. Special emphasis is made on promising new biomaterials, such as injectable bone substitute and injectable calcium phosphate cements. These materials, which combine biocompatibility, bioactivity and rheological properties, could be good alternatives in endodontics as root canal fillers. They could also be used as drug-delivery vehicles (e.g., for antibiotics and growth factors) or as scaffolds in pulp tissue engineering.

KEYWORDS: bioactivity • biomineralization • calcium phosphate • endodontics • injectable bone substitute • tissue engineering

In dentistry, endodontic therapy is performed to prevent or treat apical periodontitis. It consists of the total or partial removal of the dental pulp. The aim is to achieve healing by the formation of a mineralized tissue (dentin, osseo-dentin, cementum or osseo-cementum). The type of tissue depends on the initial pulp pathology and on the endodontic therapeutic. Endodontic procedures mainly attempt to preserve a mildly damaged pulp or promote periapical healing. Although a vital functioning pulp seems to be the more effective barrier against bacterial invasion to a certain extent [1–3], many clinicians have shown that direct pulp capping in cariously exposed permanent teeth provide unpredictable long-term results and are less successful than root canal filling [1,3–7]. This could be related to remnant bacteria in surrounding dentin despite excavation of clinical caries [1,4] as well as to the extent of the inflammatory response to the carious exposure to the pulp tissue [5,8]. In addition, it may be related to an inadequate long-term seal resulting in microorganism microleakage [4,9] or to materials that fail to favor pulp repair and dentin bridging [10–12].

The importance of pulp capping variables that mediate pulp repair activities and dentin bridge formation following pulp exposure has been assessed. The results of this study have shown that bacterial microleakage was not the only relevant factor and relationships between pulp capping materials and dentin bridge formation were observed [13]. A review has explored the biological factors contributing to the clinical success of direct pulp capping. This analysis distinguished the importance of both hemorrhage control, the removal of operative debris and biofilm at the dentin–pulp interface and a long-term 'bacteriometic' seal to avoid microleakage that can lead to pulp inflammation and necrosis [14]. Moreover, some authors believe that improvements in vital pulp therapy in cariously exposed permanent teeth should be possible in a biological perspective [15].

Concerning the root canal filling procedure, for apical periodontitis, the essential role of microbial infection is well recognized as the etiological factor. The status of the periapical tissue also has an impact on the treatment outcome [16–22,23], as well as the magnitude of the periapical pathology [24,25]. As a result, endodontic treatment is fundamentally the clinical management of a microbiological problem. The success of this therapy depends on complete disinfection through chemomechanical debridement of the pathological or necrotic pulp tissue, followed by hermetically sealing the root canal system from the oral and the periapical environment. In spite of the

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progress made in improving the performance of root canal preparation and filling techniques, the clinician is still confronted with two problems. First, the complexity of the pulp root canal and its ramifications, which create major difficulties for complete disinfection, shaping and filling in order to prevent bacterial infiltration and ingress. Second, the use of root canal filling materials that unfortunately do not meet all the requirements of an ideal material, with problems such as adhesion to parietal dentin, maintaining a sufficient seal, insolubility in tissue fluids, dimensional stability, nonresorbability, radio opacity, antibacterial activity and biocompatibility [26,27].

In addition, sealers and filling materials selected for endodontic practice have previously proven their biocompatibility in several *in vitro* and *in vivo* tests. Controversy still remains, however, regarding the acceptable biocompatibility of the main endodontic filling materials [28–30], that can hinder the process of healing in cases involving extrusion beyond the canal [26].

In recent decades, new biomaterials have been used in endodontic therapies, especially the mineral trioxide aggregate (MTA) and calcium phosphate materials. They could promote pulpal and periapical healing because of their biocompatibility and bioactive properties, thereby improve the prognosis for endodontic treatments. The question to address concerns the kind of biomaterial and conditioning that can be used in the near future. Progress in biomedical research provides new directions for the design of biologically effective pulp therapies.

This paper is a review of studies evaluating bioactive materials in endodontics with special emphasis on calcium phosphate materials, mineral trioxide aggregate (MTA), and biocompatible and biodegradable carrier vehicles for local delivery of signaling molecules to induce mineralized tissues formation.

Biocompatibility of current filling materials in endodontics

Biocompatibility tests have shown that all the currently used filling materials, including gutta percha (GP), cause local adverse effects for vital tissues [31–35].

Gutta-percha has been the most widely used root canal filling material because it was found to be well tolerated in several animal studies, where the formation of a fibrous tissue capsule surrounding pieces of GP has been reported [36–38]. However, the inertness of GP has been discussed by various authors [28–29]. *In vivo* tissue experiments show that the size, the surface character, formulation and type of GP caused cytotoxic reactions to varying extents [33–35,39,40]. Fine particles of GP (e.g., those resulting from thermocompaction techniques) cause an intense, localized tissue response that may be a significant factor in the impairment of healing of periapical lesions in the case of overfilling [35–41].

In addition, the occasionally contradictory data reported from various authors, concerning results of *in vitro* and *in vivo* studies clearly indicate that certain endodontic sealers can cause local and systemic adverse effects [28,29]. Numerous commonly used root canals sealers, such as epoxy resin-based, calcium hydroxide-based, and zinc oxide–eugenol-based sealers possess a marked cytotoxic [42,43] and tissue-irritating potency, notably for periodontal ligament cells [44,45]. Eugenol, zinc or formaldehyde products of the main root canal sealers have significant potential toxicity for periapical tissues [46–48]. In addition, root canal sealers dissolve when exposed to an aqueous environment for extended periods, possibly causing moderate or severe cytotoxic reactions and contributing to endodontic treatment failure [44,45]. Some sealers even induce necrosis of bone or cementum [49–51]. Contemporary sealers with excellent sealing and bonding properties have shown a significant cytotoxicity that generally increases with time [52]. Histological investigations on monkeys have demonstrated that root canal sealers can induce mild-to-severe periapical inflammation, especially when teeth were overfilled [53]. Recent investigations have been carried out to understand the molecular mechanisms of cytotoxicity of zinc oxide–eugenol based and epoxy resin-based root canal sealers in periapical inflammation [54,55]. Moreover, it cannot be excluded that zinc oxide sealers especially those containing formaldehyde, may pose a systemic risk and induce a toxicity for many organs of the body [30,45,51,56,57]. Mutagenic and genotoxic effects have also been observed with sealers releasing formaldehyde or generating this substance during their setting reaction [45,56], as well as with sealers containing bisphenol-A-diglycidyl-ether or its derivatives [30]. Epoxy resin-based sealers, AH26 and AH-Plus induced the highest level of DNA damage [58,59]. Furthermore, recent results on the obvious carcinogenicity of the formaldehyde-releasing and epoxy resin-based root-canal sealers on human osteoblastic cells should be taken into consideration to avoid any unexpected adverse effects in humans [43]. Although the presence of pathogens in the root canal system and a preoperative periradicular lesion are the primary cause of endodontic failure, many authors assume that the tissue response to these current root canal filling materials becomes significant in the event of overfilling and may influence the outcome of endodontic treatment [60].

Materials with potential risks of cytotoxicity, genotoxicity, mutagenicity or carcinogenicity should no longer be used in practice because safer alternatives are available.

Calcium hydroxide as a reference bioactive material?

Calcium hydroxide has good biological properties such as an antibacterial effect [61–64], and the capacity to reduce osteoclastic activity and promote mineral tissue formation (Figure 1). Its basic pH (close to 12) is due to the liberation of hydroxyl ions and is responsible for its biological properties. Calcium hydroxide in contact with connective tissue behaves as a catalyst for calcified tissue formation. The high pH can promote bone mineralization by activation of alkaline phosphatase (ALP) [65,66]. However, ALP is not the only factor involved in calcified tissue formation [67].

Used as a pulp capping agent, calcium hydroxide promotes the formation of a reparative dentin bridge [68]. The alkalinity of calcium hydroxide might be responsible for dentinogenesis [69] by

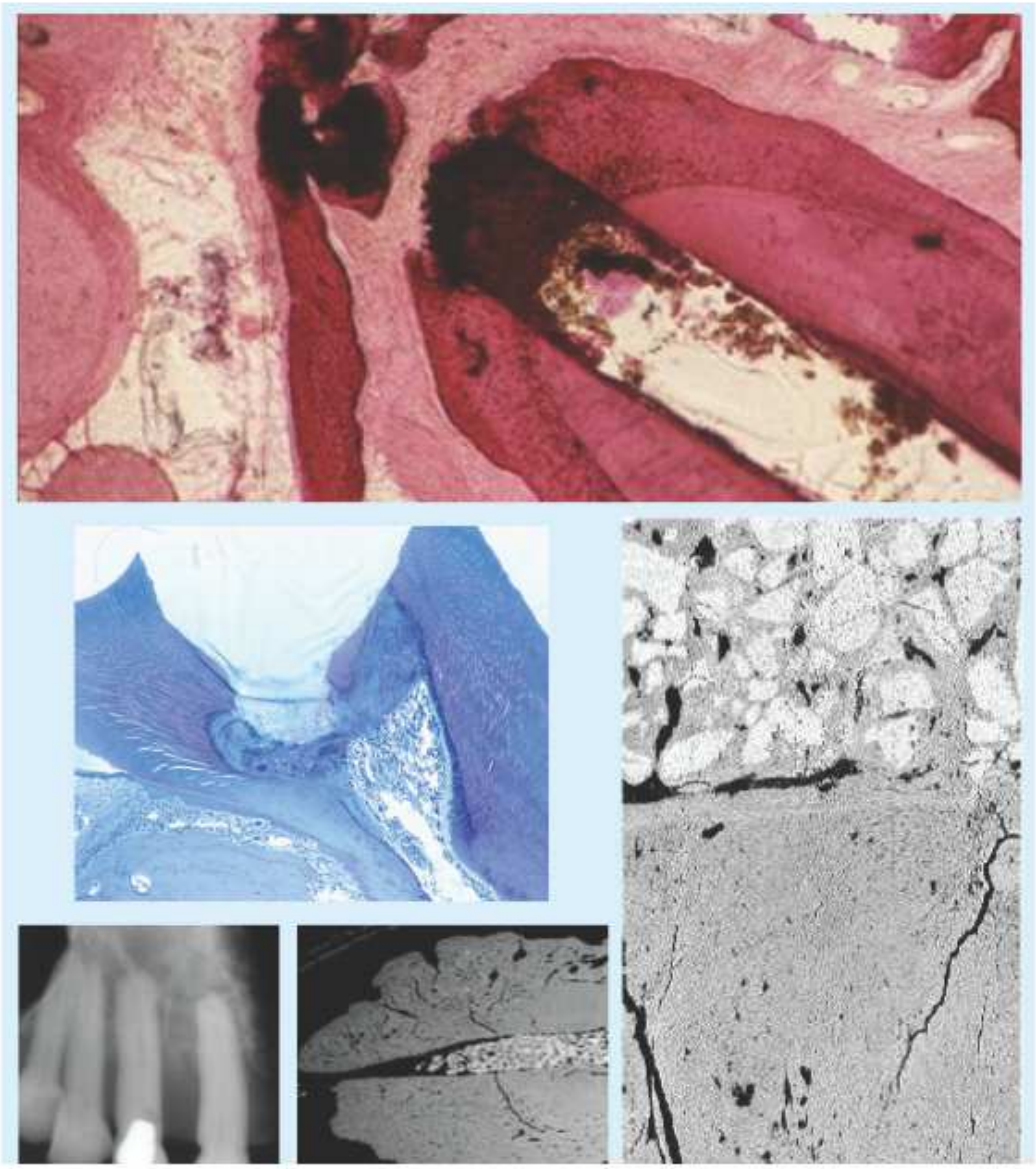

Figure 1. Histological characterizations of bioactive material in endodontics. (A) Apical healing of a dog's tooth at 3 months after filling with a calcium hydroxide paste (LM, hematoxylin and eosin). **(B)** Histology at 11 weeks post-operative after pulp capping with ProRoot MTA® (MTA). The dentin bridge is in perfect continuity with the dentine wall (LM, methylene blue/blue Azur II). **(C–E)** *In vivo* results of IBS injection in sheep model. **(C)** Radiograph radiovisiography image of the implanted zone in sheep. **(D)** The rectangular zone in **(C)**. Backscattered scanning electron micrographs of new mineral tissue formation in apical dental zone filled with IBS, 12 weeks after implantation. New mineral tissue appears in gray-like cement and dentine, IBS in white and soft tissues in black. **(E)** Enlargement of the rectangular zone in **(D)**.
c: Cementum; ca: Calcium hydroxide; d: Dentin; IBS: injectable bone substitute; l: Ligament; LM: Light microscopy; p: Pulp.
Part **(B)** with permission from Simon S and Machtou P. Parts **(C–E)** ©2006 Trans Tech Publications Ltd [301].

activating ALP. This calcified tissue is initiated by a superficial necrosis that stimulates pulp repair reactions [70]. Pulpal fibroblast-like cells also differentiate and might be responsible for the synthesis of a calcified bridge [68]. However, an *in vitro* study has demonstrated that pulp fibroblasts in contact with calcium hydroxide exhibited dramatic alterations in morphology, growth rate, protein synthesis and ALP activity [71], reflecting the necrosis observed *in vivo* [72]. Placed in direct contact with connective tissue, it promotes the formation of a cementoid barrier. However, since calcium hydroxide is soluble and degrades with time, it might not provide a permanent long-term bacteriometic seal if there is eventual failure of the restoration [9]. The development of hydrophilic adhesives creating a hybrid layer has been suggested as an alternative to calcium hydroxide as a pulp capping material to improve the long-term clinical seal against microleakage. However, the adhesive capping of exposed pulp remains controversial in terms of possible toxicity of adhesive components toward vital pulp. Several studies have reported unsatisfactory results when exposures were direct-capped with adhesives [5,12,73–75]. On the other hand, successful pulp healing and dentin bridging using adhesives have been observed in other studies [76–81]. However, in recent studies, calcium hydroxide gave a better biological performance than the self-etching adhesive [82,83]. In other endodontic procedures, calcium hydroxide allows clinical control of infection and could improve the prognosis of teeth with apical periodontitis. Some authors report a success rate of approximately 81% after 5 years of treatment of infected teeth with calcium hydroxide [84]. Nevertheless, the disadvantage of calcium hydroxide is that it must be replaced many times [85–87] in apexification and foraminal closure, which are consequently long-term procedures, requiring 6–18 months to obtain an apical barrier [85–87].

Bioactive materials as possible alternatives

Studies using bioactive materials have reported their biocompatibility and their capacity to initiate calcified tissue formation. MTA and various calcium phosphate materials are proposed as possible alternatives to current filling materials for endodontic therapy.

Mineral trioxide aggregate

Mineral trioxide aggregate is a new cement that has been developed to seal the pathway of communication between the root canal system and the periodontal tissue, and is not recommended as a complete root canal filling material [88,89]. MTA consists of calcium silicate, alumina, calcium oxide and silicate. Until 2002, only one gray-colored MTA material was available, and a white MTA (WMTA) was subsequently developed due to esthetic concerns [90]. Nontoxic properties [91,92] and biocompatibility with periapical tissues [92–94] have been demonstrated. Similar results have been obtained with MTA and calcium hydroxide in implantation tests for biocompatibility [95–99], and formation of mineralized tissues [95–97]. The mechanism for the formation of mineralized tissue involves the reaction of calcium oxides of MTA with tissue fluids to form calcium hydroxide [95–97]. The setting reaction of MTA materials might create a porous matrix characterized by internal capillaries and water channels, and the porosity and solubility of this product increase with the liquid:powder ratio [100]. According to some authors, the calcium hydroxide product of MTA materials might be responsible for their high pH level and biological properties [100–102].

MTA has antibacterial properties [103–106], probably due to its high pH. Nevertheless, these effects were observed to be lower than those of calcium hydroxide [95]. Antifungal activity of MTA against Candida Albicans was demonstrated [107], although Gray MTA (GMTA) and WMTA mixtures in various concentrations were not equally effective at preventing the growth of *Candida albicans* [108].

One of the essential characteristics required for endodontic material in both procedures is sealing ability. This property was first evaluated for repair of lateral root perforations and MTA demonstrated better results than amalgam or IRM (zinc oxide–eugenol-based cements) with the methylene blue hermeticity test [109]. As root-end filling material, MTA has a good apical sealing ability [94,110–113] that increases with time [114]. Only a small number of studies have concluded that MTA provided a sealing ability equal to that of amalgam, composite or Super EBA [115] or below that of Vitremer, Super EBA and amalgam [116]. Another study attempted to assess the factors that could affect the quality of apical seal with various root-end fillings, and although Super EBA and IRM were better than MTA regarding microleakage and marginal adaptation, it is possible that the exposure of MTA to a water-soluble dye before achieving full set and its porous microstructure contributed to these results [117].

On the other hand, *in vitro* studies reported good results in sealing open apices with MTA materials [118]. A 5 mm GMTA apical barrier was advocated, followed by a GP filling 24 h later. It was found that the MTA apical barrier resisted displacement during GP condensation. Nevertheless, calcium hydroxide pre-treatment might adversely affect white MTA sealing ability [119]. For the repair of furcation perforations, several studies concluded that MTA materials provide an efficient seal [120–122]. However, there was significantly more leakage when the perforations were challenged from the orthograde compared with the retrograde direction [123]. This result suggests the need for an effective coronal seal over MTA material to avoid an oral microleakage.

The microleakage of MTA materials has also been evaluated using bacterial penetration methods [103,105,115,124–133]. The majority of these studies suggested that MTA materials afford less bacterial leakage than traditional materials when used in retrograde filling [103,105,127,129], furcation repair [115,126] and apical closure [124,131,132]. In addition, MTA setting did not seem to be affected by the presence of blood [134]. The sealing ability of MTA, as well as its biocompatibility and its dentinogenic activity are attributed

to the production of an adherent interfacial layer that resembles hydroxyapatite in composition. The authors concluded that calcium ions released from MTA react with the phosphate ions in the tissue fluid yielding hydroxyapatite [135]. MTA supports cellular adhesion and cellular growth [136–138]. Some authors [137–139] found an increase of osteoblastic activity markers (IL-1α, IL-1β, osteocalcin and alkaline phosphatase) in contact with MTA. These results suggested that MTA would promote osteoblastic activity allowing bone tissue formation [140]. However, other authors did not obtain the same results in similar studies [141]. Although osteoblast cell growth was reported, production of IL-1α and IL-11 were not detected from the cells exposed to the gray MTA materials. Nevertheless, other cytokines involved in osteoclast recruitment (M-CSF) and osteoblastic activation (IL-6 and IL-8) were found. All of these studies highlight the osteocompatibility of MTA and the possible capacity to initiate an osteoblastic–osteoclastic process involved in bone formation and modeling. In addition, a recent study investigating the effects of MTA on cementoblast growth and osteocalcin production in tissue culture has shown that this biomaterial could be considered cementoconductive [142].

The white (WMTA) effect on dental pulp cell viability and proliferation has been assessed, with good results, on various cell lines: MDPC-23 odontoblast-like cells, OD-21 undifferentiated pulp cells [143] and human dental pulp cells [144]. Moreover, this MTA material might have a more stimulating effect on human dental pulp cells than a commercial calcium hydroxide preparation [144].

MTA bioactivity was tested in different animal models: in rats [96], guinea-pigs [145], dogs [93,146–149] and monkeys [150]. When used as a pulp capping or pulpotomy material, MTA was shown to have dentinogenic properties for example, promoting dentin bridge formation (Figure 1) [96,147,148,151–154]. When used as a root canal filling material or as a retro endodontic filling material, MTA caused little or no inflammation and induced cementum formation [93,94,146,149,150,155]. MTA has also proven its ability to induce tissue regeneration (and not only repair) in perforation treatments [150] or in retrograde fillings with a new cementum formation in animal models [146,156].

A few reported clinical cases have suggested the long-term success of this material in many endodontic procedures [89,153,157–159]. MTA appears to be an alternative for the treatment of immature or opened root apexes. Nevertheless, although numerous clinical cases have been reported using MTA to obtain an apical calcified barrier in one-visit apexification [160–168], no prospective study or controlled clinical trials have been reported. Likewise, other clinical case reports have been described using MTA successfully in vital pulp therapy [151,152,169,170], in root repairs [157,158,171–174] or as a root end filling material [175].

However, two prospective studies were performed to compare the dentinogenic effect of calcium hydroxide to those of MTA materials in pulp capping [176,177]. The first clinical study was conducted on a small sample size, using 11 pairs of third molars with mature apices [176]. GMTA specimens displayed a higher dentin bridge formation associated with a near-regular odontoblastic layer and no pulp tissue inflammation, contrary to the calcium hydroxide specimens that were characterized by a thick dentinal bridge with adjacent pulp tissue necrosis [176]. The second prospective study was a single-blinded, randomized, controlled clinical study using a larger sample size [177]. WMTA and a calcium hydroxide preparation were compared in 48 third molars, with no significant difference as regards the histologic status. These two clinical prospective studies suggest that both GMTA and WMTA perform as well as traditional calcium hydroxide in mechanical pulp exposures in teeth. Further clinical studies are required to assess the dentinogenic ability of MTA materials in carious pulp exposures.

The effectiveness of MTA for pulpotomy dressing was evaluated in several prospective studies on primary teeth with variable results [151,178–183]. Clinical assessment on permanent teeth was also performed in two studies [184–186]. The first was performed on 31 cariously exposed teeth treated by GMTA with promising results [184]. The second study reported a favorable outcome using WMTA in a private endodontic practice [186]. On the other hand, a prospective 24-month study GMTA used as a root-end filling material with 122 patients [187] reported good results, but no statistical difference was shown with the zinc oxide–eugenolate preparation.

Albeit insufficient well-designed and controlled human trials have been performed to date [87,176], although the sealing ability, biocompatibility and clinical performance of MTA in many endodontic procedures make this biomaterial one of the more relevant contemporary alternatives to the currently used endodontic materials. Nevertheless, more studies with larger samples and longer follow-up periods are suggested.

Calcium phosphate biomaterials

Over many decades, calcium phosphate biomaterials have been expected to provide additional advantages in endodontic therapy because they are biocompatible, nontoxic and can induce mineralized tissue formation. Moreover, these biomaterials are bioactive since they can elicit specific tissue responses [188–193], depending on their dissolution–reprecipitation and biodegradation–bioresorption [190,191,193]. These processes are of primary importance for neo-osseous formation or dentin bridging. Partial dissolution of calcium phosphate ceramics leads to precipitation of apatite microcrystals in the center and on the surfaces of the biomaterial. The calcium phosphate biomaterials also sustain cellular degradations (phagocytosis and osteoclasis) and are replaced by new hard calcified tissue. The biomaterial can favor the osteoconduction process by its porosity, allowing colonization of either bone or the dental pulp implantation site by osseous cells such as osteocytes and osteoblasts. The calcium phosphate biomaterials act as scaffolds for the formation of new mineralized tissue.

Based on these biological properties [188,193–196], the use of calcium phosphate materials in endodontic therapy as potential alternatives to current materials was proposed in the late 1970s [196]. The need for a biocompatible material that would provide either an apical seal or a coronal 'bacteriometic' seal had therefore already been recognized [98,197–199] as being necessary for long-term success

in endodontic treatments [14]. Calcium phosphate materials are able to create a tight bond with mineralized tissues [188,194,196,200,201], which could warrant an effective barrier against bacterial leakage in the apical area as well as in the dentin–pulp interface. Several authors have emphasized the use of materials that improve the long-term clinical seal in direct pulp capping [9].

Calcium phosphate ceramics

Calcium phosphate ceramics in powder forms are nowadays of historical interest but many reported applications have distinguished their bioactivity and their sealing ability in endodontic procedures, including pulp capping [202], apexification [203–205] and endodontic surgery [206]. During the 1980s and 1990s, many *in vivo* studies explored the use of different types of calcium phosphates in pulp-capping, seeking to induce new dentin formation without an initial necrotic fibrous layer and to avoid pulpal cell alterations usually observed using $CaOH_2$ [71]. Satisfactory results were reported with the hydroxyapatite (HA), tricalcium phosphate (β-TCP), biphasic calcium phosphate (BCP; an intimate mixture of HA and β -TCP), octacalcium phosphate (OCP), and dicalcium phosphate dihydrate (DCPD) [72,201,207–214]. HA is idealized as the inorganic component of calcified tissues. DCPD, OCP and β-TCP are able to transform in to apatites similar to biologic apatites [200].

In vivo studies evaluating the dentinogenic effect of calcium phosphate ceramics on animal models reported three types of mineralization: dentin bridge formation, dystrophic calcification and mineralization.

Microparticles of β-TCP, HA and BCP are responsible for the formation of a calcified bridge similar to that observed with calcium hydroxide, although success was more frequently obtained with HA and BCP [201,212,215]. β-TCP or HA used as pulp capping materials in human trials generally reported good results [72,207,213,216]. OCP and DCPD evaluated on various animal models caused extensive dystrophic mineralized tissue in the pulp chamber and also along the root canal walls [212,215]. Using macroparticles of β-TCP, HA or BCP in animal models, homogenous mineralization was observed around the biomaterials [210,212,214]. These results were in agreement with conclusions obtained in human trials with HA [213]. The homogenous mineralization was closely bonded with the dentinal walls and showed intimate bone contact by a process described as osseocoalescence by Daculsi *et al.* in 1990 [194].

These histological observations suggested that calcium phosphate ceramics may be useful for specific applications in endodontics: microparticles of HA, TCP, BCP for pulp capping and macroparticles of HA, OCP, DCPD for pulpotomy and apexification procedures [201,212,215]. A recent study showed that OCP-based cement allowed favorable healing processes in pulp capping in a rat model [214]. The efficiency of TCP was tested in the treatment of root perforations [207,217]. Although it was less toxic than calcium hydroxide, this material did not perform as expected. The results obtained in apexification using HA [218] or generic TCP [219,220] and apexogenesis using β-TCP [203,221,222] were more convincing. β-TCP is resorbable, allowing bone and cement growth to progressively close the apical foramen, although the generic TCP requires intimate dentin contact. According to these studies, calcium phosphate ceramics are biocompatible towards periapical tissues and the authors recommended their use in apical barrier formation [203,218–222].

Calcium phosphate cements

The concept of apatitic calcium phosphate cement (CPC) was first introduced by LeGeros in 1982 [223]. The first patent on hydraulic CPC (self-setting or self-hardening) was obtained by Brown and Chow in 1988 [224]. In the 1990s, important efforts were made to develop injectable bone substitutes (IBS).

The CPCs were first used as bone substitutes to repair craniofacial defects. The histological observations on animal models [225,226] showed a bone-implant interface with proliferation of osseous cells in the volume of the implant after several weeks, and then a slow reduction of the biomaterial with new bone formation after several months.

According to their great dimensional stability and their biocompatibility towards soft and hard tissues [227–232] and especially towards the periapical area [232–235], CPC was proposed for use in pulp capping [236], endodontic sealing and filling [225,231–235,237–242]. These preclinical studies concluded that CPC can promote wound healing in the periapical tissue [234,235]. In a monkey model, CPC deliberately extruded in the periapical area created minimal inflammation with deposition of new bone. Ossification of the nidus in the mass of CPC was observed [235]. In a rat model, the cement placed in the root canal caused apical closure with a cementum-like calcified product [232].

Since the development of the hydroxyapatite cement by Brown and Chow in 1986, many types and generations of CPC have been perfected [227,230,231,235,240,241,243–249]. New self-setting CPCs containing calcium oxide (CaO) or calcium hydroxide were also developed [250]; these biomaterials might be an interesting alternative to calcium hydroxide, which is currently used in endodontics. A mono calcium phosphate monohydrate-CaO-based cement was recently proposed for endodontics treatment with better mechanical properties than calcium hydroxide. The setting reaction produced a mixture of calcium-deficient hydroxyapatite (CDHA) and calcium hydroxide, calcium hydroxide making this cement more suitable for endodontic applications than orthopedic ones. The presence of calcium hydroxide would confer antibacterial properties to this CPC [236,251]. In the same way, by mixing DCPD and CaO, a CPC with better mechanical and physical properties for dental applications was obtained. This DCPD–CaO based cement provided a better sealing than the one obtained using zinc oxide–eugenol cement with or without GP point. In addition, this cement also presented antibacterial effects due to the presence of calcium hydroxide [252–254]. Another composite material consisting of MTA with CPC matrix was also developed as a root-end filling material to combine the qualities (biological properties, sealing ability [255]) of each biomaterial and to improve its manipulation.

Its chemical properties and biocompatibility are similar to those of MTA. In addition, chitosan-based cements, which are non-rigid cellulosic cements, were evaluated and the preliminary results on their bioactivity, and biocompatibility showed that they could be promising for various dental applications such as endodontics [256].

Injectable calcium phosphate cements

The size and the lack of accessibility of the various endodontic sites require the development of injectable forms. The thick consistency of CPC makes it unfit for injection [246]. Various formulations were proposed to improve their handling. For example, addition of substances such as glycerine [233–235,257], silicon gel [240], polyethylene glycol, liquid paraffin, glycerol [231,258], cellulosic [232,242,258–260] or TiO_2 [241] compounds can increase the rheological properties and control the setting time. To promote periapical tissue healing, the addition of another gelling agent, chondroitin sulfate, was also proposed in CPC formulation [228,241]. The latest studies by Chow and coworkers have recently resulted in water-free formulation of CPC: these premixed CPC pastes are stable in the package and harden after being delivered to the osseous site where glycerol-tissue fluid exchange occurs [258].

This aqueous solution is a biological polymer (e.g., collagen) or a synthetic polymer (e.g., cellulosic ethers, dextran, chitosan). Others components, such as dispersants, binders, plasticizers or drugs, can be incorporated to modify their biological properties and their injectability. Unlike CPC, injectable ceramics do not have intrinsic primary mechanical properties after the setting reaction. Mechanical strength results from a rapid and physiological bone formation in the center of the biomaterial [261,262].

A collagenic gel was first proposed in association with the mineral component, both to improve the handling and the injectability of the calcium phosphate ceramics and for its biological properties. Collagen is an extracellular matrix protein involved in mineralization processes, such as apatite and bone formation [263,264].

Studies with animal models were conducted with injectable paste that can be easily placed in the canal [232–235,241]. Microporosity of such biomaterial favors the exchange of tissue fluids between canal and parietal dentin, without bacterial colonization. Several *in vivo* studies were made with CPC used as a sealer in association with GP [237,252,265]. CPC was more biocompatible and induce a less inflammatory reaction compared with zinc oxide-eugenol sealer [266]. Nevertheless, many authors have evaluated the cement injected with syringe in the root canal as a filler on animal models [232–235,241].

The various studies carried out to test the apical seal ability gave contradictory results, probably due to the various immersion media used and also due to the CPC formulation and extrusion properties [257]. Scanning electron microscope analysis reported that apical and dentinal tubule occlusion appeared to be similar both with CPC and Grossman's cement sealer [238]. Some animal studies showed that CPC had a uniform and tight adaptation to the dentinal surfaces of the pulp chamber and root canal walls [216,233]. On the other hand, another study reported that the CPC sealer does not provide as good an apical seal as Grossman's cement [237]. The relatively poor performance of CPC used as a sealer in laterally condensed GP might be due, in part, to the experimental conditions [67,257]. In another study, the apical seal of CPC sealer used with vertical condensation of warm GP was not inferior to that observed with Grossman's cement [240]. However, the single cone CPC procedure provided an adequate apical seal against dye penetration, which was not significantly different to laterally condensed GP filling [265].

As a general rule, the different CPC formulations proposed for complete root canal filling offer a great sealing quality [227,233,241,242,257]. Moreover, the excellent apical sealing ability and the apatitic product of CPC make them suitable for furcation perforation repair [267] or for root end fillings [230,268]. A recent study concluded that CPC used as root-end material would have a sealing ability comparable to MTA [111].

Calcium phosphate cements are efficient at stimulating an apical barrier formation [232] and can be a possible alternative to the long-term apexification procedure [257,269]. A successful clinical case of apical barrier formation has been reported [270] in a nonvital permanent tooth with an open apex communicating with the maxillary sinus.

In endodontics, a composite material of calcium phosphate and collagenic gel was first tested on monkeys in 1977 and 1978 in apexification [271,272], and in pulpotomy and partial pulpectomy to induce the physiological canal space closure [273]. Other animal studies reported successful results using composite materials of calcium phosphate and collagen in apical barrier formation [274]. This composite gel was shown to promote pulp calcification. Nontoxic and biocompatible, it was resorbed and replaced by mineralized tissues that looked like dentin or cementum. This gel was also evaluated in a clinical study in apexogenesis and in root canal overfilling [275]. Biomaterial extrusion in the infected periapical area produced disappointing results. According to the authors, this failure was due to bacterial contamination of the apical dentin and cement. Although the collagen is biocompatible and can promote the formation of calcified tissues, such biological components might be responsible for contaminations (e.g., prion contamination with the bovine collagen) and a synthetic polymer gel might be a preferable alternative.

Development of an injectable bone substitute

Based on the good results reported with both calcium phosphate ceramics and CPC in involving calcified tissues formation, the development of a composite bioactive material was carried out. This material is an injectable ceramic (IBS) consisting of biphasic calcium phosphate in a matrix of hydroxypropylmethyl cellulose [276]. The biocompatibility of cellulose and its derivatives has been documented [276,277].

The main attractive feature of this injectable biomaterial is the mineral component with various HA:β–TCP ratios making it possible to control its kinetics of dissolution and precipitation, and, subsequently, the bioactivity of the bone substitute [190,191,223,278–280]. The degradation of the cellulosic polymer and the stability of this composite material were evaluated [281–284]. CPCs provide dense biomaterials with irregular microporosity [244], whereas macroporosity is known to be an essential factor for homogeneous and early bone colonization [285–287].

The *in vivo* behavior and the bioactivity of this injectable biomaterial was first studied in the context of osteoformation. Although CPC showed good direct contact with newly formed bone, it was slightly degraded 3 weeks after implantation [288] and the cells were unable to penetrate into the CPC biomaterial and to produce a complete mineralized tissue substitution [289]. In contrast to CPC, which has a primary hardening reaction and a slow substitution rate, bone ingrowth with IBS becomes greater at the expense of the biomaterial, as porosity and interconnections increase [290]. Moreover, the injectable ceramics favor an earlier and more extensive osteogenesis than large BCP ceramic granules and provide an osseous architecture with progressive but early improvement in mechanical properties [291]. *In vitro* cytotoxicity studies and *in vivo* biocompatibility studies showed that the composite materials do not cause adverse host reactions [276,292].

This injectable BCP/polymer composite material, or IBS, was first used with success on dog models on vertebral disk sites [293] and to fill periodontal pockets or bone alveolar sockets [294]. Other *in vivo* studies were carried out with various animal models [290–292,295].

These *in vivo* studies showed that IBS supported extensive bone colonization [289,290,294] and the newly formed bone was in perfect continuity with the trabecular host bone structure [262]. These promising results were recently confirmed on bone sockets in a human clinical trial [296].

In endodontics, the difficulty in injecting ceramic through a thin needle relates to the water used as the liquid-phase carrier. However, injectable calcium phosphate biomaterials would be able to pass through thin needles and dental root canals without alteration or demixing of the phases. Water or liquid phases without viscous consistency show Newtonian properties and an aqueous polymer solution is a better carrier for mineral granules. Apparent viscosity measurements and extrusion tests have indicated that macromolecules are most suitable for this purpose. An injectable composite IBS (80–200 µm) consisting of a 2% aqueous cellulose ether solution and biphasic calcium phosphate granules of 80–200 µm have been tested. The cellulosic gels are pseudoplastic and their viscosity decrease with the shearing during the extrusion from the syringe, and increase after injection. Extrusion experiments showed that the best carrier had a heavy molecular weight [283]. A study comparing CPC, IBS (80–200 µm) and IBS (40–80 µm) has shown that both materials were injectable but had different flow characteristics [289]. The CPC extrusion profiles indicated better properties than the IBS with smaller BCP granules (40–80 µm) for injection through large needles. However, with thin needles, the extrusion of CPC was impossible but IBS (40–80 µm) was injected without demixing.

To develop an injectable composite for endodontics, small calcium phosphate granules are preferable for injection in a narrow root canal. Few studies have been conducted on the role of particle size of calcium phosphate ceramic on wound healing and calcified tissue ingrowth and have shown conflicting results [209,297,298]. In pulp capping, 300 µm granules of HA and β-TCP would provide greater hard tissue formation than 40 µm ones [297], whereas in bone filling, small HA particles would be more efficient [209]. In the case of IBS, consisting of a mixture of various grain sizes, the effect of the particle size was of great importance. An *in vivo* evaluation of various grain sizes of biphasic calcium phosphate was performed to elucidate the role of granulometry in ceramic resorption, bone ingrowth and inflammatory reactions; three particle sizes were compared: 10–20, 80–100 and 200–400 µm [299]. This study revealed different behaviors of the BCP powders. Inflammatory responses, bone ingrowth and ceramic degradation were different depending on the BCP grain size. BCP particles of 10–20 µm appeared to provide suitable granulometry to promote bone ingrowth and large particles for bone bonding. Other *in vivo* studies have investigated the biological effects of IBS with various particles sizes: 40–80, 80–200 and 200–500 µm [262,295,300]. These studies confirmed that small calcium phosphate particles (40–80 µm) support bone ingrowth to a similar extent to larger ones. The BCP degradation and the bone substitution process occurred earlier and faster for IBS 40–80 µm than for IBS 200–500 µm [300]. Qualitatively, IBS with small BCP particle granulometry was shown to be more favorable for restoration of the initial trabecular structure [295]. IBS (40–80 µm) seemed to be an efficient biomaterial to induce new bone and calcified tissues formation but could also facilitate the injection in narrow sites as dental root canals. IBS 40–80 µm was recently evaluated in an *ex vivo* and *in vivo* study [301] to fill dental root canal after total removal of canal pulp in an animal model (Figure 1). The results showed that injection is possible with a high amount of BCP granules in the apical zone for extracted teeth. In sheep models, the dental apex is large and bleeding is difficult to stop after pulpectomy, which is a negative parameter to allow a good filling. Despite the low level of granules in the apical zone, a new mineral apposition was always observed after 12 weeks, which confirms the sealing ability by bone ingrowth of IBS in this animal model.

These preliminary results obtained with BCP/hydrosoluble polymer composites, described as IBS, demonstrated that they could be used in endodontics as a possible root canal filling material. However, further *in vivo* investigations, as well as clinical studies, are needed to assess the performances of this new injectable bioactive material in everyday endodontic procedures.

Expert commentary

The range of biomaterials in dental surgery, especially in endodontics has increased since in recent years; research in this field have evaluated the response of various calcium phosphate biomaterials to both many therapeutic indications (e.g., pulp capping, pulpectomy, apexification, root repair, a retro root canal filling) and to the main biological and technical requirements of the clinician (e.g., bioactivity and ease of use). The efficacy of such materials has been demonstrated in many *in vivo* studies but additional long-term controlled studies are needed to ensure their clinical benefits in endodontics.

In addition, research with biomaterials in this field needs to address some important questions in the next few years, especially from an economic perspective. At the present time, the expensive cost of commercial biomaterials has limited their application to the treatment of complex and/or special cases.

Is the main expectation for the future in endodontics to spread the use of biomaterials for all treatments (even those that have a high percentage of success with current techniques) or to focus the research on the treatment of cases with a very bad prognosis?

In the final analysis, an ideal therapy would consist of regenerative approaches as tissue engineering that will possibly involve the treatment of the whole pathological case in endodontics and cover all therapeutic indications.

Five-year view

Tissue engineering & drug delivery devices

The field of tissue engineering has been developed over the last 10 years to recreate functional, healthy tissues and organs in order to replace diseased or dead tissues. Tissue engineering has opened new directions in the design of methods of endodontic treatment, aimed at regeneration of the dentin–pulp complex [302–305].

Strategies employed to engineer tissue can be categorized into conductive, inductive and cell transplantation approaches [302–304]. A common feature of all of these strategies is the use of biomaterials. The conductive approach requires passive biomaterials as a barrier membrane to exclude connective tissue cells that will interfere with the regenerative process. The inductive approach employs a biodegradable polymer scaffold as a vehicle to deliver bioactive molecules directly (with growth factors) or indirectly (with genes that encode these proteins) to the host site [306,307]. Biodegradable polymer carriers can release, at a controlled rate, bioactive proteins to promote the formation of the desired tissue [303].

The cell transplantation strategy uses a similar polymer vehicle for delivery of cells and even partial tissues to the anatomic site to guide new tissue formation. A variety of new biomaterials are being developed for these applications. Injectable materials that allow minimally invasive delivery of inductive molecules or cells are very attractive [284,289,292,296,301,303,308].

In endodontics, the regeneration of dentin and dental pulp has been achieved *in vitro* and in animal studies using tissue engineering. There are potentially several ways to engineer lost dentin and dental pulp [305,309].

The induction of reparative dentine or the mineralization of the pulp with BMPs, extracellular matrix molecules and tissue engineering after pulp capping and pulpotomy are under consideration with various animal models [302,310–322]. Several bioactive molecules have been studied *in vivo* by direct implantation into the pulp of rats to assess their role in the formation of reparative dentin [309,311,323–325] and in the proliferation of dental pulp stem cells [326,327]. These studies have shown that bioactive molecules could promote the first step towards pulp repair. There is now evidence suggesting that even if the odontoblasts (cells that produce dentin) are lost, it may be possible to induce formation of new cells from pulp tissue using BMPs or extracellular matrix proteins [313,314,319,328]. The new odontoblasts can regenerate dentin. Dental pulp engineering and cell transplantation approaches are also under consideration, using cultured fibroblasts, pulp stem cells, morphogens and polymer matrices [329–334]. More recently, the possible use of gene therapy of BMPs for endodontics has been studied [335,336].

In the last 10 years, the treatment possibilities in endodontics have increased with the introduction of new injectable polymer biomaterials, such as IBS, that could also be used as drug-delivery vehicles [337] for antibiotics [338,339] or growth factors [306,340,341]. The molecules absorbed on the device must be released after implantation, according to well-defined kinetics. Antibiotic incorporation in an IBS would be useful to promote periapical tissue healing in the treatment of apical lesions in which the prognosis is uncertain. The simplest approach to pulp tissue healing would be regeneration of the lost pulp tissue. However, attempts to regenerate pulp tissue under conditions of inflammation or partial necrosis have proved unsuccessful [342]. Several case reports have documented revascularization of necrotic root canal systems by disinfection followed by establishing bleeding into the canal system via overinstrumentation [343,344]. These findings suggest that revascularization of necrotic pulps with closed apices might require both the complete disinfection of the root canal [345,346] and a large instrumentation of the tooth apex to allow systemic bleeding into root canal systems. The formation of a blood clot yields a matrix of fibrin that traps cells capable of initiating new tissue formation. This approach might be useful in regenerative endodontics and plasma-derived fibrin clots have been used for the development of scaffolds. In a case report, platelet-rich plasma gel (PRP), in conjunction with TCP, has been recently proposed for the treatment of a periapical inflammatory lesion. PRP consists of thrombocyte concentrates and high amounts of growth factors sych as PDGF, IGF and TGFβ that are important in wound healing and regeneration [347]. Revascularization might be one of the main challenges of regenerative endodontics involving stem cells, growth factors and matrix scaffold.

Despite the considerable evolution of the tissue regeneration approach, some of these techniques to regenerate pulp tissue are at a very early stage of development. Additional research and clinical trials are needed to elucidate their efficacy and safety.

In the future, tissue engineering and drug-delivery systems such as injectable biomaterials may consequently change everyday practice in endodontics because they offer an alternative to save teeth that may have compromised structural integrity.

Conclusion

Bioactive materials have given proof of their efficiency in inducing mineralized tissue in endodontics, both in animal studies, clinical cases reports and human trials. Some of them, such as MTA, are actually used in special clinical indications: in apexification, in root repairs or as a root-end filling material. Moreover, for pulpectomy and total root canal filling, new injectable biomaterials that combine biocompatibility, bioactivity and rheological properties could be a good alternative in endodontics to current root canal filling materials. One of the great expectations of the next decade is the development of clinical applications of drug delivery systems and tissue engineering that promise to promote both periapical tissue healing in the treatment of apical lesions and dentin bridging in pulp capping, for which prognosis is the worst.

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Key issues

- Endodontic therapy is performed to prevent or treat apical periodontitis. The success of this therapy depends on complete disinfection through chemomechanical debridement of the pathological pulp tissue, followed by the hermetic sealing of the root canal system. However, the clinician is confronted with, first, the complexity of the root canal pulp and its ramifications that make it difficult to efficiently achieve its disinfection, preparation and filling, and second, the use of filling materials that are harmful to periapical tissues.
- The range of biomaterials in dental surgery, especially in endodontics has increased in recent years; mineral trioxide aggregate and calcium phosphate biomaterials have been assessed as biocompatible and bioactive alternatives to current filling materials in endodontics. They have demonstrated their efficiency in inducing some mineralized tissues in endodontics.
- To improve their ease of use, an important evolution in this field was observed with the development of various injectable calcium phosphate biomaterials. Composite biomaterials such as injectable bone substitutes (consisting of calcium phosphate in a polymer matrix) could have the necessary qualities for root canal filler in endodontics. They combine biocompatibility, bioactivity and the rheological properties to be injected in a narrow root canal.
- Currently, special emphasis is made on a new therapeutic approach based on tissue regeneration. Injectable bone substitutes could find a place in regenerative endodontics as drug delivery devices and as scaffolds in pulp tissue engineering.

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Epilogue.

L'analyse de la littérature concernant les nouveaux axes de recherche et le développement de biomatériaux nous a permis d'entrevoir les champs d'applications possibles de matériaux bioactifs et du tissu engineering dans le domaine de l'endodontie. Ces nouvelles perspectives pourraient changer radicalement les thérapeutiques des pathologies pulpaires et périapicales dans un avenir plus ou moins proche.

Néanmoins, la promesse de telles alternatives suscite d'autres questions: pourront-elles apporter un bénéfice thérapeutique réel par rapport aux thérapeutiques endodontiques conventionnelles ? Quel est le cahier des charges d'un biomatériau à vocation endodontique, notamment face au problème récurrent de la contamination bactérienne ?

Ceci impose une analyse de la survie des traitements endodontiques à moyen et long terme et l'identification des facteurs pronostiques déterminants.

Partie II : Cohorte rétrospective

Lorsque nous avons commencé ce travail, nous souhaitions tout d'abord estimer la proportion d'échecs thérapeutiques obtenus auprès de la patientèle du Centre de Soins Dentaires de NANTES. La littérature scientifique internationale révèle alors des taux de succès importants lorsque le traitement est réalisé dans le respect de bonnes pratiques cliniques, laissant entendre que le bénéfice obtenu avec un biomatériau serait négligeable. Cependant, la majeure partie de ces résultats sont obtenus à partir de traitements réalisés par des spécialistes chevronnés de l'endodontie.

De plus, encore peu d'études multivariées étaient alors réalisées pour l'identification des facteurs prédictifs du succès du traitement endodontique, dont le pronostic est pourtant plurifactoriel.

Il semblait donc primordial de mettre en place une cohorte longitudinale nous permettant d'obtenir, à partir d'une analyse multivariée, des informations sur la proportion d'échecs et les facteurs de risque des traitements endodontiques réalisés au Centre de Soins Dentaires.

Cette étude, dont le recueil des données initiales est rétrospectif, permettra d'obtenir *relativement* rapidement les résultats préliminaires à l'élaboration d'une seconde étude pronostique de l'endodontie, *i.e.* une cohorte prospective sur grand échantillon.

1. Matériels et Méthode :

1.1. Objectifs :

Cette première étude a pour objectif principal d'évaluer dans le temps le pronostique des thérapeutiques endocanalaires réalisées au Centre de Soins et de Traitements Dentaires-CHU Hôtel Dieu de Nantes, à partir d'une cohorte de patients ayant bénéficié d'un ou plusieurs traitements au moins un an auparavant.

L'objectif secondaire est l'analyse de l'influence de différents facteurs sur la réussite ou l'échec de nos traitements : mettre en évidence un effet praticien, un effet dent, un effet techniques et protocole utilisés ou un effet qualité d'obturation endodontique et coronaire.
Pour répondre à ces objectifs, nous avons utilisé un modèle d'analyse de survie multivariée, le **modèle de Cox**.

1.2. Hypothèses de travail :

Nous avions plusieurs hypothèses de travail à explorer, conformément aux résultats rapportés par la littérature [19, 83, 84] :

- La probabilité de réussite des traitements endodontiques réalisés au Centre de Soins Dentaires avec des protocoles standardisés et des techniques de référence serait supérieure 0,80 à un an pour une population indemne de pathologie périapicale initiale. Cette probabilité de succès diffère avec l'existence d'une pathologie périapicale au moment du traitement, ainsi que selon le niveau et la qualité de l'obturation canalaire.
- Différents facteurs liés au niveau de compétence de l'intervenant (étudiants de second cycle, internes ou praticiens) aux techniques de préparation et d'obturation

endocanalaires, à la dent (difficultés d'accès, nombre de canaux) pourraient influer sur le succès de nos traitements endodontiques.

1.3. Population étudiée :

Nous avons étudié la population traitée par endodontie au centre de soins dentaires, HOTEL DIEU durant les années universitaires 1999-2000 et 2000-2001.

Nous avons pu recruter notre échantillon à partir de fiches d'évaluation établies pour chaque traitement endodontique, soit1066 fiches au total.

503 patients ont bénéficiés d'une ou plusieurs thérapeutiques endodontiques durant cette période (avec 2.12 endodonties par patient en moyenne). Tous les patients du listing ainsi obtenu ont été contacté pour une consultation de suivi une année au moins après la fin de leur traitement.

Nous avons fait le choix de ne pas faire un tirage au sort à partir du listing, étant donné que le recrutement se fait sur la base du volontariat et que la plupart des patients susceptibles d'être inclus dans l'étude ont terminés ou ont interrompus leurs soins bucco-dentaires. Afin d'obtenir un échantillon suffisamment grand, nous avons contacté l'ensemble des patients.

1.4. Critères d'évaluation :

Le recueil des données rétrospectives concernant la pathologie initiale et le traitement se fera à partir du dossier clinique (feuilles de soins endodontiques, radiographies du soin évalué).

Concernant les données socio-démographiques du patient et les données cliniques obtenues lors de la consultation de suivi, un questionnaire et une fiche de recueil ont été réalisés *(cf. annexes).*

Succès/Echec du traitement endodontique [53, 99]

L'évaluation clinique et radiologique de l'endodontie à 1 an minimum après réalisation du traitement endodontique s'appuie sur les critères définis ci-dessous :

Population indemne de pathologie périapicale initiale	**Population avec pathologie périapicale initiale**
Echec : -Apparition de signes cliniques tels que des douleurs provoquées ou spontanées, une fistule, une voussure vestibulaire ou palatine révélant une pathologie d'origine endodontique -Apparition de signes radiologiques avec un score PAI≥ 2 (Peri Apical Index scoring system) [105] -Dent non fonctionnelle ou extraite	***Echec : non rémission d'une pathologie périapicale préexistante.*** -Apparition de signes cliniques tels que des douleurs provoquées ou spontanées, une fistule, une voussure vestibulaire ou palatine révélant une pathologie d'origine endodontique -Augmentation du volume de l'image radioclaire avec augmentation de l'indice PAI. -Dent non fonctionnelle ou extraite
Succès : -Absence de signes cliniques et radiologiques avec un PAI≤ 1 -Dent fonctionnelle	***Succès :*** -Absence de signes cliniques -Régression notable ou disparition totale de l'image radioclaire de la lésion apicale avec PAI≤ 2, signant une cicatrisation périapicale complète ou subtotale. - Dent fonctionnelle
Cas incertain : -Signes cliniques inconstants, de faible intensité et intermittents dont l'origine n'est pas clairement déterminée (origine endodontique non prouvée)	***Cas incertain :*** -Signes cliniques inconstants, de faible intensité et intermittents - Non régression notable de l'image periapicale radioclaire

***Tableau 1** : Critères d'évaluation clinique et radiographique des thérapeutiques endodontiques.*

Les travaux de Reit en 1987 [99] ont montré qu'il fallait attendre un délai d'un an pour savoir si le traitement était soit un succès, soit un échec ou encore un cas incertain. Les traitements incertains devront être réévalués à 4 ans.

La difficulté de l'évaluation des traitements endodontiques vient du fait qu'elle ne se fait pas grâce à un critère binaire classique succès / échec. Le temps étant un paramètre variable dans cette évaluation, nous avons voulu analyser le pronostic des thérapeutiques au moyen de données censurées.

1.5. Facteurs prédictifs possibles du résultat thérapeutique :

- Facteur **dent** : paramètres renseignant sur la localisation, le nombre de canaux et la complexité canalaire.
- Facteur **praticien** : niveau de compétence du soignant.
- Facteur **protocole** : champ, nombre de séances de traitement, état de la restauration coronaire.
- Facteur **techniques** de préparation et obturation.
- Facteur **qualité d'obturation** : concordance entre niveau d'obturation et longueur de travail, qualité de la condensation.

Les facteurs étudiés sont ceux décrits dans la littérature [60, 66, 68].

1.6. Analyse statistique :

1.6.1. Nombre de sujets :

Il s'agit d'une étude d'observation longitudinale rétrospective et le nombre de patients ne peut donc être défini à l'avance, d'autant plus que le suivi des patients repose sur le volontariat. Néanmoins, afin d'obtenir une évaluation suffisamment précise de la valeur pronostique des différents facteurs étudiés sur nos thérapeutiques endodontiques, nous envisagions une inclusion d'une centaine de patients environ.

1.6.2. Evénement attendu et événement censurés :

1.6.2.1. Population indemne de pathologie périapicale

L'échec est l'évènement habituellement observé dans les analyses de survie. Il correspond par ailleurs à la réalité clinique, puisque le praticien va être attentif à l'apparition de symptômes ou d'une image de raréfaction osseuse signant l'échec du traitement endodontique.

L'échec est donc l'événement enregistré pour l'analyse. Tout autre événement comme le succès thérapeutique et les cas incertains sont censurés (à droite), c'est-à-dire qu'ils sont enregistrés comme l'absence d'évènement observé.

1.6.2.2. Population avec pathologie périapicale initial

Bien que l'événement observé dans les quelques travaux publiés sur la survie des thérapeutiques endodontiques soit l'échec [57, 59, 61, 62] , il nous semble également intéressant de suivre dans le temps la régression des images radiographiques de pathologie périapicale jusqu'à cicatrisation complète.

Dans un premier temps, l'évènement attendu sera l'échec et les évènements censurés seront les cas incertains et les succès.

Dans une deuxième analyse, l'évènement attendu sera le succès (cicatrisation complète ou subtotale) et les évènements censurés seront les cas incertains et les échecs thérapeutiques.

Les cas incertains ou états intermédiaires de cicatrisation ne pourront donc influer sur les résultats thérapeutiques étudiés: échec thérapeutiques ou cicatrisation périapicale complète. Ce choix d'analyse vient de la constatation que l'échec en endodontie et la perte de dents traitées endodontiquement n'est pas *stricto senso* l'évènement contraire du succès ; les éventuels facteurs de risque de l'échec ne seront pas forcément les facteurs protecteurs de la cicatrisation apicale.

1.6.3. Estimation :

Estimations ponctuelles au moyen de pourcentages, moyennes et écart-types pour les variables qualitatives et quantitatives.

Vérification de l'homogénéité des 2 groupes au niveau de leur répartition selon l'âge, le sexe, *(tests de t student)* et des catégories socio-démographiques *(test du Chi^2).*

1.6.4. Analyse univariée :

Les analyses consisteront à tester l'existence d'une relation entre les variables étudiées prises séparément et la réussite ou l'échec du traitement endocanalaire au moyen d'un *test du Log Rank.*

1.6.5. Analyse multivariée :

Les facteurs qui auront été précédemment identifiés dans les analyses univariées comme liés à la réussite ou à l'échec du traitement endocanalaire avec un seuil de signification à $p<0.20$ seront ensuite incorporés dans un *modèle de Cox.* L'utilisation de méthodes de sélection pas à pas ascendantes ou descendantes permettra de sélectionner les facteurs pronostiques des thérapeutiques endodontiques avec un seuil de signification à $p<0.05$.

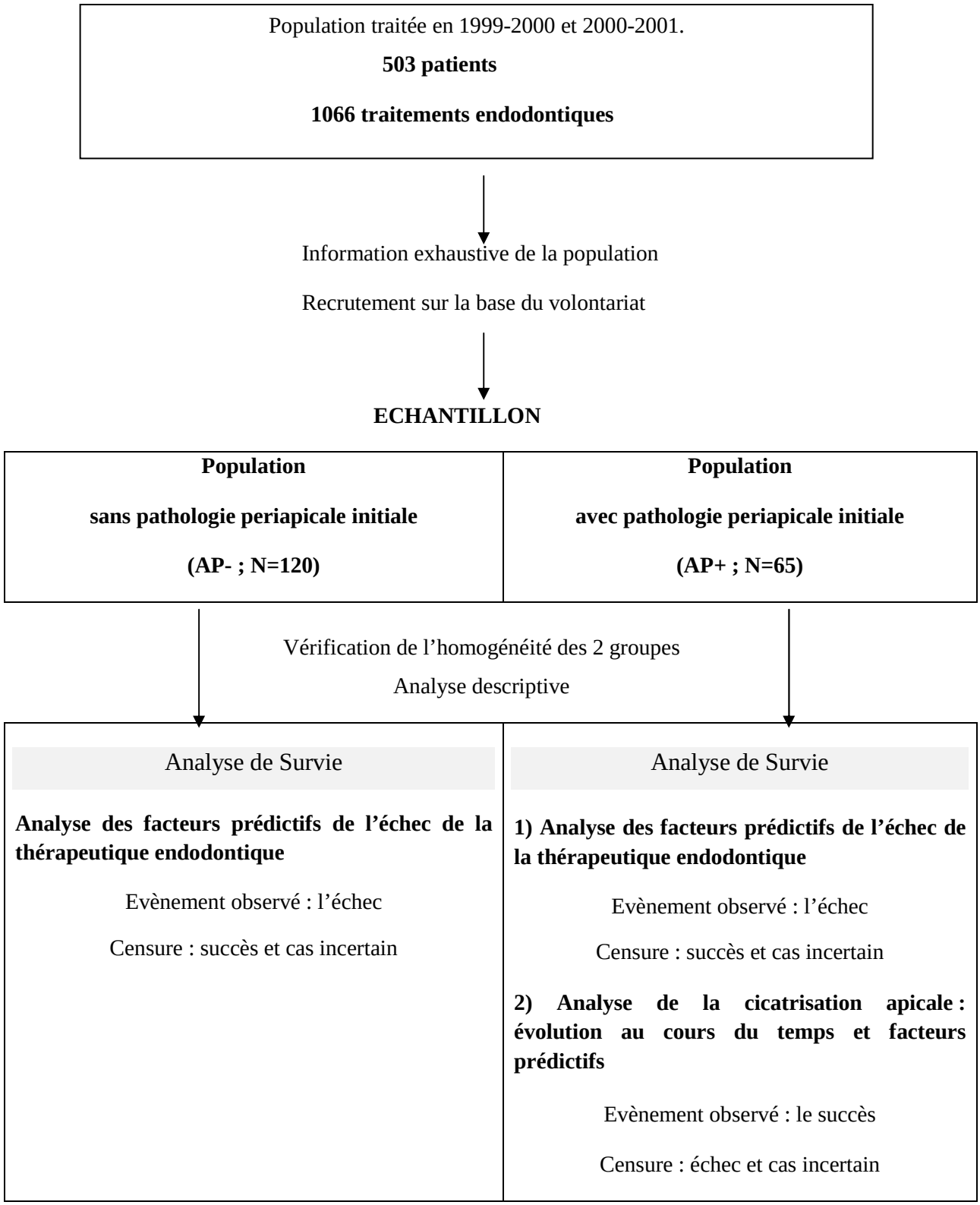


Figure 1 : *Méthodologie de la cohorte rétrospective.*

2. Résultats :

Sur les 503 patients ayant bénéficié de traitements endodontiques, plus d'un tiers sont perdus de vue ou exclus de l'étude: 169 ont déménagé ou n'ont pas d'adresse connue et 2 sont décédés. Parmi les 332 patients restant, 241 ne souhaitaient pas participer à l'étude ou n'ont pas répondu à la convocation.

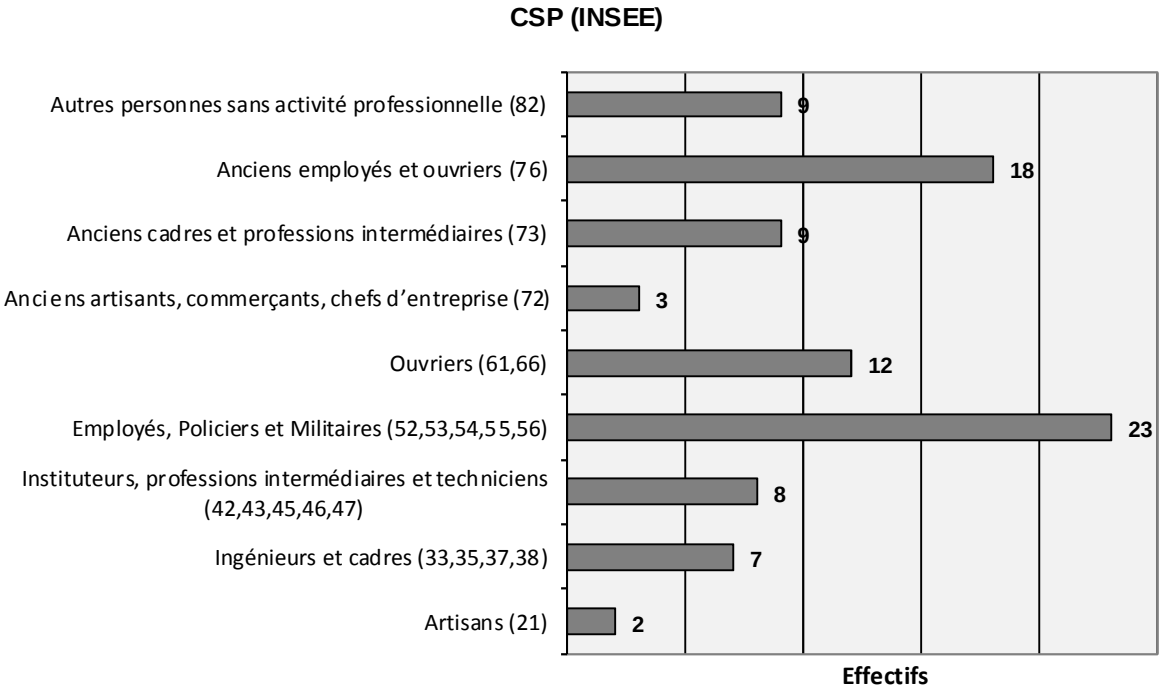
Nous avons donc obtenu un échantillon de 91 patients, ce qui représente un taux de réponse à l'enquête de 27.4% (91 sur 332 patients). Au total, 185 traitements endodontiques ont été évalués dont 120 réalisés sur dents sans pathologie périapicale (groupe AP-) et 65 sur dents avec pathologie périapicale (groupe AP+).

La période de suivi (période entre la fin du traitement et la consultation) est de 121.28 ± 39.24 semaines. Le délai de réévaluation des traitements endodontiques s'échelonne de 1 à 4 ans.

2.1. Caractéristiques sociodémographiques de l'échantillon :

	Population indemne de pathologie périapicale au départ **AP-** **N=120**	**Population présentant une pathologie périapicale au départ** **AP+** **N=65**
Age	*56,44 ±15,638*	*53,6 ±16,129*
Nationalité française	*98,8%*	*99%*
Sexe: Hommes	*37,28%*	*31,84%*
Femmes	*62,72%*	*68,16%*

Tableau 2*:Caractéristiques socio-démographiques des patients participant à l'étude.*



***Graphique 1**: Catégories Socio-Professionnelles des patients inclus dans l'étude.*

L'analyse des caractéristiques démographiques et socioprofessionnelles met en évidence une population dont la moyenne d'âge est de 54 ans (54.04 ± 16.47), à majorité féminine **(**61.5% de femmes contre 38.5% d'hommes) et de nationalité française (98.9%) *(cf. tableau 2).* Les catégories socioprofessionnelles (CSP) les plus représentées sont les ouvriers et professions intermédiaires en activité ou à la retraite *(cf. graphique 1).*

2.2. Analyse descriptive des paramètres étudiés :

Les 2 groupes AP- et AP+ présentent des caractéristiques similaires, sans différence statistiquement significative par rapport à la population source *(cf. tableaux 3a et 3b).* L'homogénéité et la représentativité des 2 groupes AP- et AP+ sont donc respectées.

***Tableau 3a**: Répartition des facteurs pronostiques étudiés (en fréquences et pourcentages)*

	AP-		AP+		Chi² p-value	Population totale	
	n	**%**	**n**	**%**		**n**	**%**
Localisation de la dent traitée							
antérieure	*65*	*54 %*	*44*	*68 %*	*0.0742*	*109*	*59 %*
postérieure	*55*	*46 %*	*21*	*32 %*		*76*	*41 %*
Type de dent							
monoradiculée	*47*	*39 %*	*34*	*52 %*	*0.0854*	*81*	*44 %*
pluriradiculée	*73*	*61 %*	*31*	*48 %*		*104*	*56 %*
Calcification/Obstacle canalaire							
absence	*109*	*92 %*	*58*	*89 %*	*0.5963*	*167*	*91 %*
présence	*10*	*8 %*	*7*	*11 %*		*17*	*89%*
Niveau d'obturation							
correct (de 0,5 à 1,5 mm en deçà de l'apex radiographique)	*67*	*56 %*	*33*	*52 %*	*0.5796*	*100*	*54 %*
incorrect	*53*	*44 %*	*31*	*48 %*		*84*	*46 %*
Correspondance entre longueur de travail et longueur d'obturation							
présence	*88*	*84 %*	*51*	*93 %*	*0.1126*	*139*	*87 %*
absence	*17*	*16 %*	*4*	*7 %*		*21*	*13 %*
Re-traitement (RTE)							
absence (traitement initial)	*76*	*63 %*	*24*	*37 %*	***0.0006***	*100*	*54 %*
présence (RTE)	*44*	*37 %*	*41*	*63 %*		*85*	*46 %*
Niveau de compétence							
internes et étudiants de 3ème cycle	*27*	*24 %*	*8*	*13 %*	*0.0821*	*35*	*20 %*
étudiants de 2nd cycle	*86*	*76 %*	*54*	*87 %*		*140*	*80 %*

	AP-	AP+	Chi² p-value	Population totale

	n	%	n	%		n	%
Médication							
aucune	*29*	*24 %*	*12*	*18 %*	*0.6323*	*41*	*22 %*
hydroxyde de calcium	*61*	*51 %*	*37*	*57 %*		*98*	*53 %*
autre	*30*	*25 %*	*16*	*25 %*		*46*	*25 %*
Nombre de séances de traitement							
obturation immédiate	*63*	*53 %*	*33*	*52 %*	*0.9426*	*96*	*53 %*
plusieurs séances de traitement	*56*	*47 %*	*30*	*48 %*		*86*	*47 %*
Technique de préparation canalaire							
préparation manuelle	*112*	*93 %*	*61*	*94 %*	***1***	*173*	*93 %*
rotation continue	*8*	*7 %*	*4*	*6 %*		*12*	*7 %*
Restauration coronaire							
correcte	*101*	*89 %*	*51*	*84 %*	*0.8667*	*152*	*87 %*
défectueuse ou absente	*13*	*11 %*	*10*	*16 %*		*23*	*13 %*
Courbure canalaire							
absente ou faible	*86*	*72 %*	*52*	*80 %*	*0.2139*	*138*	*75 %*
courbure significative	*34*	*28 %*	*13*	*20 %*		*47*	*25 %*
Sur-obturation (apex anatomique ou au delà)							
absente	*107*	*90 %*	*55*	*87 %*	*0.5916*	*162*	*89 %*
présente	*12*	*10 %*	*8*	*13 %*		*20*	*11 %*
Sous-obturation (≥ 2 mm en deçà de l'apex)							
absente	*77*	*65 %*	*40*	*63 %*	*0.8708*	*117*	*64 %*
présente	*42*	*35 %*	*23*	*37 %*		*65*	*36 %*

Tableau 3b*: Moyenne et dispersion des facteurs pronostiques quantitatifs étudiés dans les 2 groupes*

	AP-	**AP+**	*t student valeur p*
Temps de suivi en semaines			
Minimum	26(*)	42(*)	*0.516*
Maximum	185	219	
Moyenne	117	125	
Ecart-type	41.5	36.81	
Nombre de séances de traitement			
Minimum	1	1	*0.966*
Maximum	7	7	
Moyenne	2.51	2.56	
Ecart-type	1.34	1.44	
Nombre de canaux			
Minimum	1	1	*0.088*
Maximum	4	4	
Moyenne	2.08	1.81	
Ecart-type	0.95	0.94	

TEST de LILLIEFORS non significatif : variables quantitatives normales

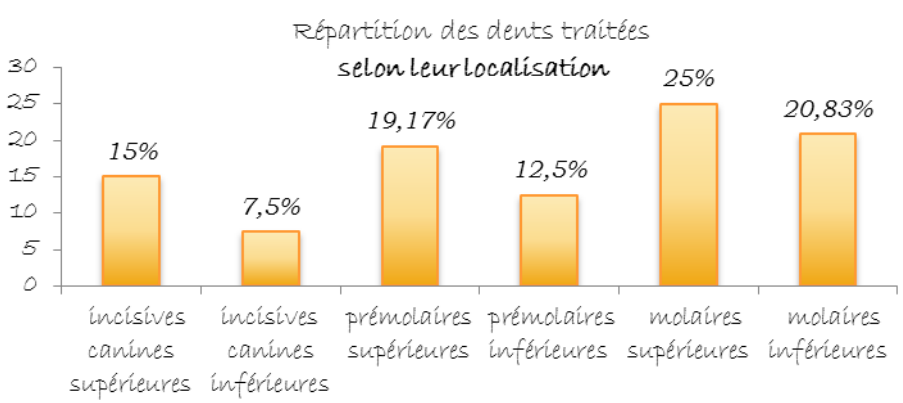
***Tableau 4** : Résultats des traitements endodontiques de chaque groupe selon les recommandations de l'European Society of Endodontology.*

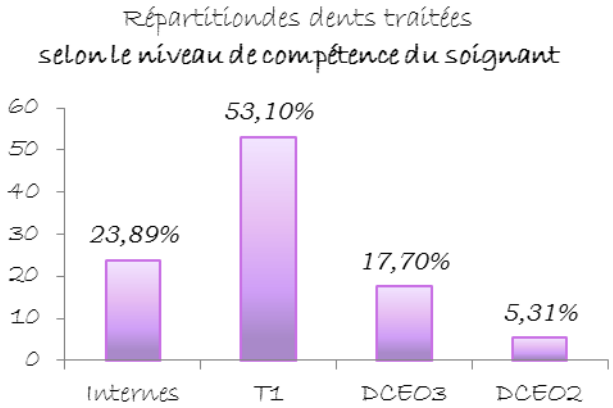
	Sans pathologie périapicale initiale (AP-) n=120	Avec pathologie périapicale initiale (AP+) n=65	Comparaison entre les 2 groupes (Chi^2) p value
Echec	*10.8% (13)*	*15.4% (10)*	*0.370*
Succès	*89.2% (107)*	*67.7% (44)*	*<0.001*
Cas incertain ou cicatrisation periapicale inachevée		*16.9% (11)*	*<0.001*

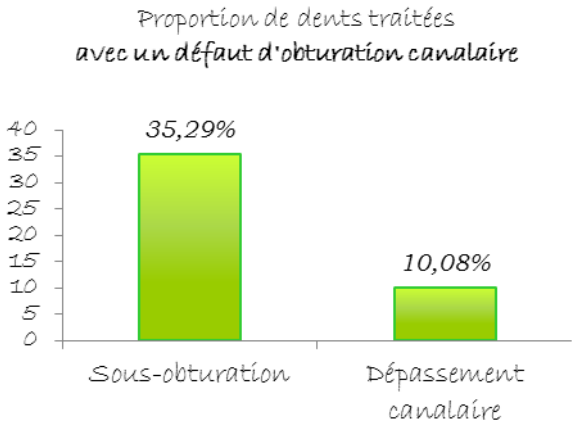
Au terme de l'étude, le succès thérapeutique est observé pour 89.2% des dents traitées sans pathologie périapicale initiale contre 67,7% des dents avec pathologie périapicale. Dans le groupe AP+, 11 cas sont incertains et demanderont un suivi pendant 4 ans.

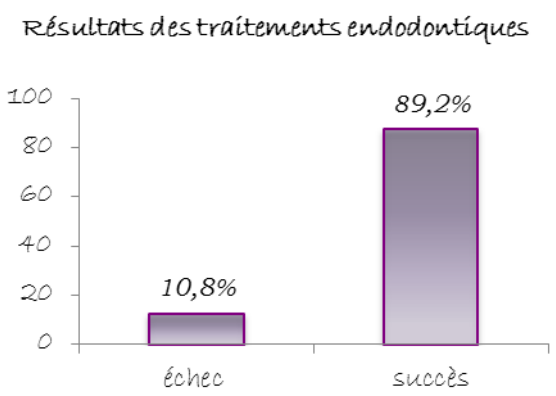
La répartition des facteurs pronostiques étudiés semble similaire dans les 2 groupes AP- et AP+ (tableau) à l'exception du facteur *Retraitement*. L'échantillon sans pathologie périapicale initiale a bénéficié de 63% de traitements initiaux contre 37% pour celui ayant une pathologie périapicale initiale *(p=0.0006*). La durée moyenne de suivi n'est pas statistiquement différente entre les 2 groupes, puisqu'elle est de 2 ans et 3 mois ± 9 mois dans le groupe AP-, et de 2 ans et 5 mois ± 8 mois dans le groupe AP+. L'obturation immédiate ainsi qu'un niveau d'obturation correct concernent la moitié des traitements endodontiques réalisés. Nous observons également que seule une minorité de dents ont été préparées avec un système Nickel-Titane en rotation continue (moins de 10%).

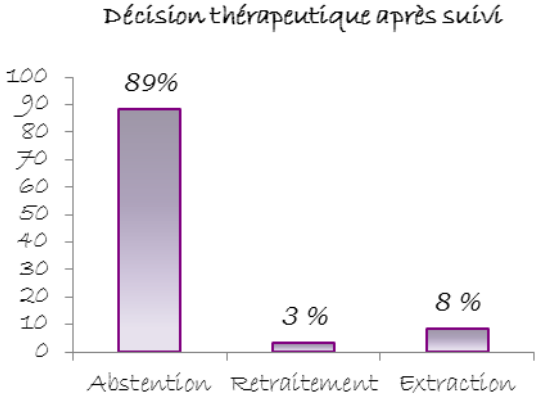
Graphiques 2 a, b, c, d, e : *Résultats obtenus dans la population* ***sans pathologie périapicale initiale (AP-)***



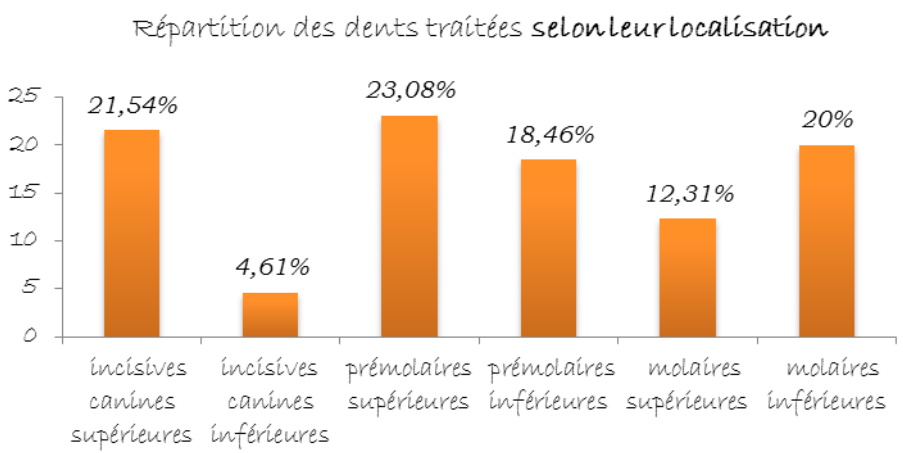


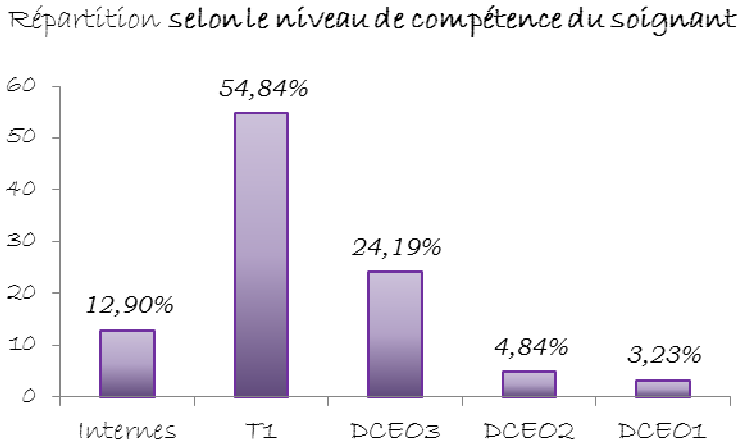


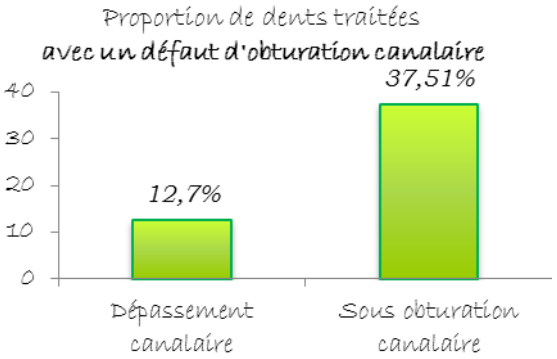


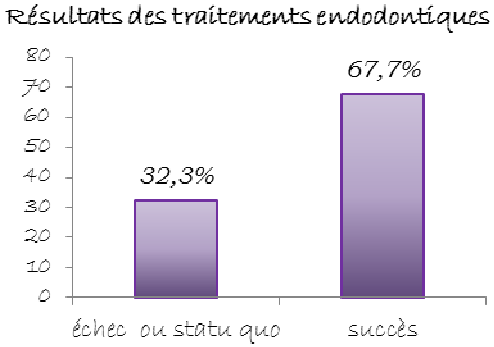


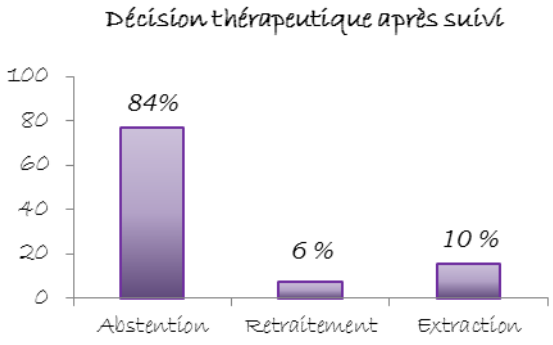
Graphiques 3 a, b, c, d, e : *Résultats obtenus dans la* ***population avec pathologie périapicale initiale (AP+)***





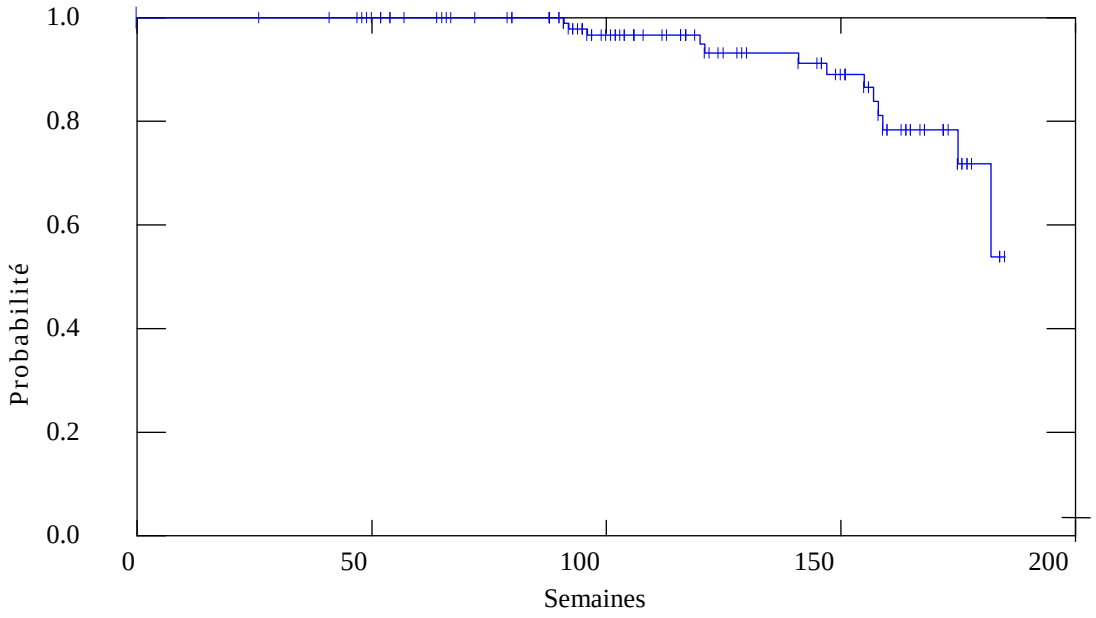






2.2.1. Population sans pathologie périapicale avant traitement (AP-) :

Graphique 4: Probabilité de survie des traitements endodontiques des dents sans pathologie périapicale initiale (AP-)

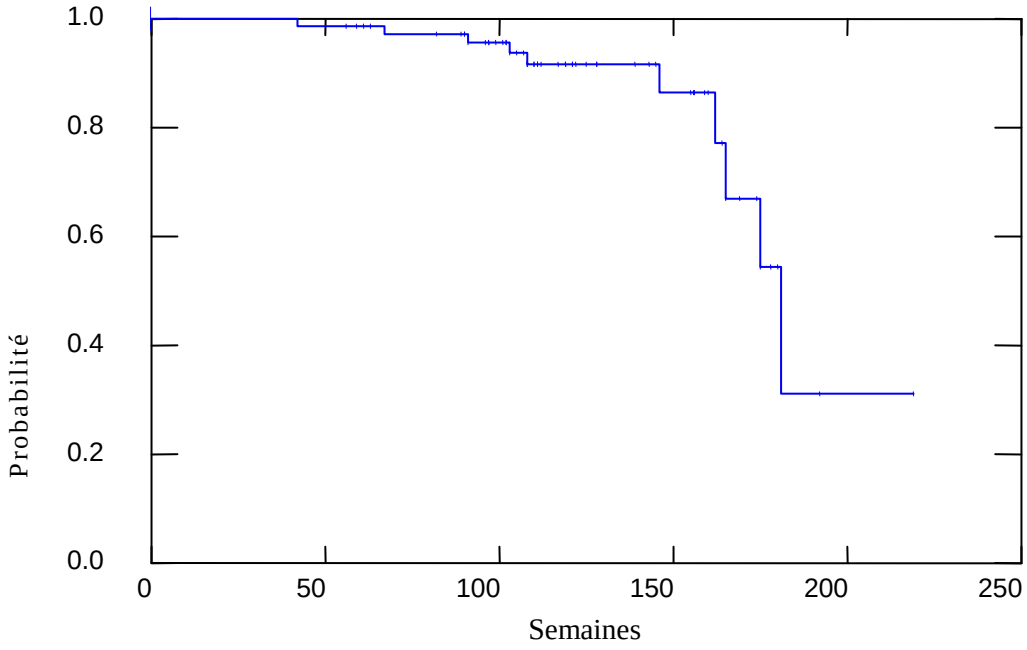


Courbe de survie: *la probabilité de survie décroit de 91 à 182 semaines, période pendant laquelle tous les échecs sont observés.*

La courbe de survie *(Graphique 4)* pour le traitement endodontique des dents sans pathologie périapicale initiale. (AP-) montre que les 13 échecs sont survenus entre 91 et 182 semaines après traitement (soit presque de 2 à 3 ans et demi). 9 dents ont été extraites et 5 retraitées. Parmi les dents extraites, 4 avaient soit des symptômes ou une pathologie périapicale, soit avaient été extraites pour raison parodontale ou pour indication prothétique. Seules 6 dents traitées parmi les 13échecs thérapeutiques recensés avaient une restauration coronaire adaptée, raison pour laquelle les échecs observés étaient tardifs (au-delà de 1 an)

2.2.2. Population avec pathologie périapicale avant traitement (AP+) :

Graphique 5: Probabilité de survie des traitements endodontiques des dents avec pathologie périapicale initiale (AP+)



Courbe de survie: *la probabilité de survie décroit de 42 à 181 semaines, période pendant laquelle tous les échecs sont observés.*

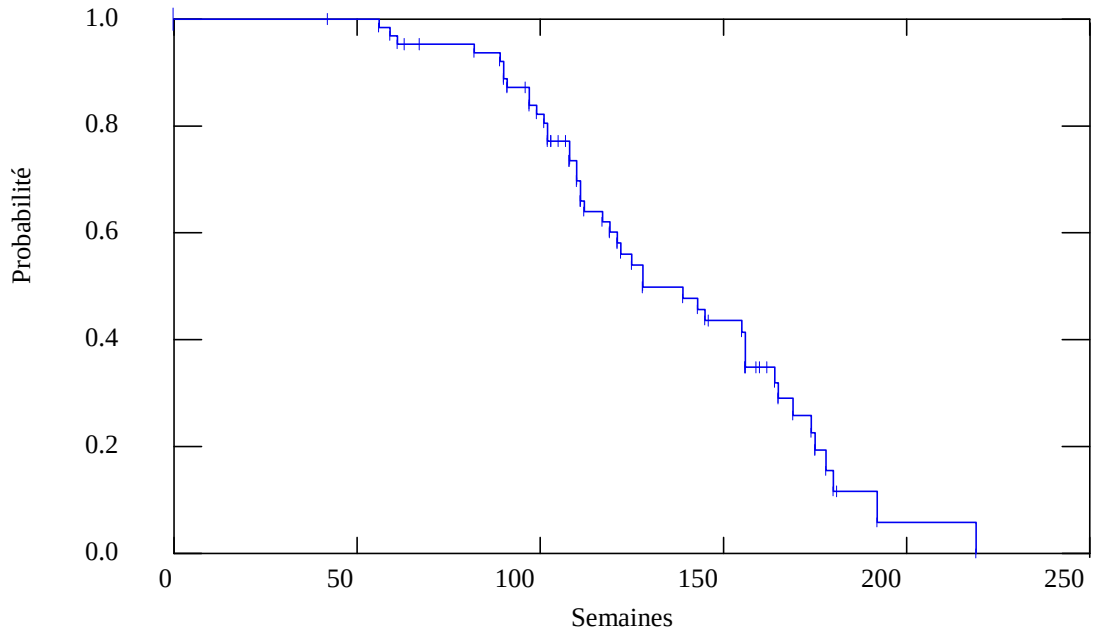
Dans ce groupe, les 10 échecs sont observés entre 42 et 181 semaines après traitement, soit dès le 9ème mois jusqu'à 3 ans et demi *(Graphique 5).* A 1an, la probabilité de survie est encore de 0.987 avec 1 seul échec sur 10 observé. A 2 ans, elle est de 0.937 avec 4 échecs sur 10.

Au terme de l'étude, 7 dents ont été extraites et 3 retraitées dans la population de dents avec pathologie périapicale initiale. Parmi les 7 dents extraites, 5 d'entre-elles avaient une restauration coronaire défectueuse ou absente, entrainant des lésions carieuses secondaires et l'impossibilité de restaurer les dents traitées. Pour l'une des 2 autres dents traitées,

l'extraction a été motivée par l'absence de cicatrisation périapicale ; pour l'autre, l'indication d'extraction (survenant à 42 semaines) n'a pas été clairement renseignée. Les 3 retraitements (à la fois orthogrades et chirurgicaux) sont liés à l'absence de rémission de la lésion initiale.

Au total, 4 échecs sur 10 ont une origine endodontique dans le groupe AP+.

Graphique 6: Probabilité d'échec ou de cicatrisation incomplète des dents traits avec pathologie périapicale initiale (AP+)



Courbe de survie: *La probabilité d'absence de cicatrisation ou de cicatrisation périapicale incomplète décroit de 56 à 219 semaines, période durant laquelle tous les succès avec disparition totale de l'image radioclaire sont observés.*

La cicatrisation périapicale s'achève sur une période allant de 42 semaines (9 mois) à 219 semaines (4 ans révolus) *(Graphique 6).* A 42 semaines, une seule cicatrisation sur 54 est observée ; à 2 ans, 15 dents traitées présentent une régression totale ou sub-totale de leur lésion apicale. La probabilité d'avoir des cicatrisations incomplètes ou des échecs à cette période est encore supérieure à 0.8.

2.3. Analyse de survie :

L'analyse univariée grace à des tests de Log Rank permet d'évaluer de l'implication de chaque paramètre, ***indépendamment les uns des autres***, sur :

- l'apparition de pathologie périapicale pour le groupe AP-
- l'échec thérapeutique pour le groupe AP+
- la cicatrisation apicale pour le groupe AP+

A partir de ces tests univariés, nous obtenons une sélection de variables significatives qui sont intégrées dans des modèles multivariés de Cox où ***les variables sont évaluées ensemble***. Par méthode pas à pas ascendante et descendante, nous obtenons un modèle de Cox final avec un ensemble de variables impliquées dans le succès ou l'échec thérapeutique des 2 populations AP- et AP+. Pour éviter toute colinéarité, certains facteurs comme *la santé périapicale actuelle* et *la décision thérapeutique* (directement liées à *l'évolution*) n'ont pas été intégrés dans les modèles de données de survie.

Par ailleurs, la *technique d'obturation* et la *technique de préparation* ont été retirées de l'analyse multivariée puisque la majorité des cas a été traitée avec préparation manuelle et condensation latérale, les autres techniques n'ayant été utilisées de façon marginale que pour le traitement de cas complexes et par des étudiants de 3ème cycle uniquement *(biais d'indication).*

2.3.1. Population sans pathologie périapicale avant traitement (AP-) :

Pour l'analyse du lien entre les différents facteurs pronostiques et l'évolution défavorable du traitement ou l'apparition de pathologie périapicale, l'événement étudié est **l'échec**. Les succès et les cas incertains seront considérés comme absence d'évènement.

Tableau 5*: Tests du Log Rank pour la mise en évidence des facteurs liés à l'échec thérapeutique dans le traitement endodontique des dents sans pathologie périapicale initiale. (AP-)*

FACTEURS	Degré de liberté (ddl)	Test de Tarone –Ware	Valeur de p
Situation maxillaire ou mandibulaire	*1*	*0.000*	*0.996*
Situation antérieure ou postérieure	*1*	*1.069*	*0.301*
Retraitement endodontique	*1*	*1.938*	*0.164*
Niveau de compétence des étudiants	*3*	*11.383*	***0.010***
Médication d'inter-séance	*2*	*0.531*	*0.767*
Obturation immédiate	*1*	*0.269*	*0.604*
Niveau d'obturation LO	*1*	*5.364*	***0.021***
Correspondance entre LO et LW	*1*	*1.717*	*0.190*
Etat coronaire	*1*	*12.992*	***<0.001***
Nombre de canaux (mono *vs* pluricanalaire)	*1*	*0.608*	*0.436*
Présence de courbure canalaire	*1*	*0.332*	*0.565*
Présence de calcification canalaire	*1*	*0.086*	*0.770*
Présence de sur-obturation canalaire	*1*	*0.139*	*0.709*
Présence de sous-obturation canalaire	*1*	*5.187*	***0.023***
Technique de préparation	*1*	*0.865*	*0.352*

Tableau 6*: Modèle de Cox final : facteurs liés à l'échec thérapeutique dans le traitement endodontique des dents sans pathologie périapicale initiale. (AP-)*

Paramètres	Estimation du hazard ratio	Intervalle de confiance (95%).	t-ratio	p
Différence entre LO et LW	2.837	(1.643 ; 4.031)	2.377	*0.017*
Restauration coronaire défectueuse	3.270	(2.111 ; 4.429)	2.820	*0.005*
Dents monocanalaires	2.501	(1.208 ; 3.794)	2.071	*0.038*

Pour le groupe AP-, l'analyse univariée fait apparaitre un lien significatif entre l'échec thérapeutique et 4 facteurs : le niveau de compétence des étudiants *(p=0.010)*, un niveau d'obturation endodontique incorrect *(p=0.021)*, une restauration coronaire défectueuse ou absente *(p<0.001)* et la présence de sous-obturation canalaire *(p=0.023) (cf. tableau 5).*

Le modèle de Cox final *(cf. tableau 6)* met en évidence 3 facteurs prédictifs de l'échec de la thérapeutique endodontique de dents sans pathologie périapicale initiale :

- l'absence d'étanchéité coronaire *(p=0.005)*, responsable d'une forte proportion d'échecs dans ce groupe.
- l'absence de correspondance entre le niveau d'obturation et la longueur de travail *(p=0.017).*
- les dents pluricanalaires par rapport aux monocanalaires *(p=0.038)*

2.3.2. Population avec pathologie périapicale avant traitement (AP+) :

2.3.2.1. Facteurs liés à l'échec thérapeutique :

Tableau 7: *Tests du Log Rank pour la mise en évidence des facteurs liés à l'échec thérapeutique dans le traitement endodontique des dents avec pathologie périapicale initiale. (AP+)*

FACTEURS	ddl	Test de Tarone –Ware	Valeur de p
Situation maxillaire ou mandibulaire	*1*	*5.319*	***0.021***
Situation antérieure ou postérieure	*1*	*2.355*	*0.125*
RTE	*1*	*0.263*	*0.608*
Niveau de compétence des étudiants	*3*	*2.891*	*0.409*
Médication d'interséance	*2*	*0.389*	*0.823*
Nombre de séances de traitement	*3*	*0.728*	*0.867*
Niveau d'obturation	*1*	*4.457*	***0.035***
Correspondance entre LO et LW	*1*	*0.749*	*0.387*
Etat coronaire	*1*	*5.503*	***0.019***
Nombre de canaux (mono *vs* pluricanalaire)	*1*	*1.537*	*0.215*
Présence de courbure canalaire	*1*	*0.013*	*0.910*
Présence de calcification canalaire	*1*	*4.826*	***0.028***
Présence de Sur-obturation canalaire	*1*	*1.703*	*0.192*
Présence de Sous-obturation canalaire	*1*	*4.477*	***0.034***

Tableau 8: *Modèle de Cox final : facteurs liés à l'échec thérapeutique dans le traitement endodontique des dents avec pathologie périapicale initiale. (AP+)*

Paramètres	Estimation du hazard ratio	Intervalle de confiance (95%).	t-ratio	p
Restauration coronaire défectueuse	2.126	(1.409 ; 2.843)	2.964	0.003
Présence de calcification ou d'obstacle canalaire	2.097	(1.145 ; 3.049)	2.204	0.028

Pour le groupe AP+, l'analyse univariée *(cf. tableau 7)* fait apparaitre un lien significatif entre l'échec thérapeutique et 5 facteurs : le nombre de canaux *(p<0.001)*, un niveau d'obturation endodontique incorrect *(p=0.035)*, une restauration coronaire défectueuse ou absente *(p=0.019)*, la présence de calcification canalaire *(p=0.028)* et la présence de sous-obturation canalaire *(p=0.034)*.

Le modèle de Cox final *(cf. tableau 8)* met en évidence 3 facteurs prédictifs de l'échec de la thérapeutique endodontique de dents sans pathologie périapicale initiale :

- l'absence d'étanchéité coronaire *(p=0.003)*
- la présence de calcification ou oblitération canalaire *(p=0.028)*

2.3.2.2. Facteurs liés à la cicatrisation périapicale :

Pour la réalisation de l'analyse des données de survie, l'événement attendu dans ce cas précis est le **succès** et le « non-événement » regroupe les échecs et cas incertains.

Tableau 9*: Tests du Log Rank pour la mise en évidence des facteurs liés à la cicatrisation périapicale dans le traitement endodontique des dents avec pathologie périapicale initiale. (AP+)*

FACTEURS	ddl	Test de Tarone –Ware	Valeur de p
Situation maxillaire ou mandibulaire	*1*	*0.076*	***0.783***
Situation antérieure ou postérieure	*1*	*0.168*	*0.682*
RTE	*1*	*2.565*	*0.109*
Niveau de compétence des étudiants	*3*	*12.585*	***0.006***
Médication d'inter-séance	*2*	*1.544*	*0.462*
Nombre de séances de traitement	*4*	*0.775*	*0.942*
Obturation immédiate	*1*	*0.414*	*0.520*
Technique de préparation	*1*	*6.526*	***0.011***
Niveau d'obturation	*1*	*1.363*	*0.243*
Correspondance entre LO et LW	*1*	*0.024*	*0.878*
Etat coronaire	*1*	*0.040*	*0.842*
Nombre de canaux	*1*	*1.693*	*0.193*
Présence de courbure canalaire	*1*	*0.431*	*0.511*
Présence de calcification canalaire	*1*	*0.010*	*0.919*
Présence de sur-obturation canalaire	*1*	*0.339*	*0.560*
Présence de sous-obturation canalaire	*1*	*2.507*	*0.113*

Tableau 10: *Modèle de Cox final : facteurs liés à la cicatrisation apicale dans le traitement endodontique des dents avec pathologie périapicale initiale. (AP+)*

Paramètres	Estimation du hazard ratio	Intervalle de confiance (95%).	t-ratio	p
Sur obturation	-1.603	(-2.229 ;-0.913)	-2.322	*0.020*
Dent monocanalaire	1.121	(0.729 ; 1.513)	-2.864	*0.004*
Correspondance entre LO et LW	1.210	(0.826 ; 1.594)	3.149	*0.004*
Niveau d'obturation correct	-2.680	(-3.602 ;-1.758)	-2.906	*0.002*

La cicatrisation périapicale semble favorisée par: la technique de préparation canalaire utilisée *(p<0.001)* et le niveau de compétence des étudiants *(avec une valeur au seuil de signification, p=0.054) (cf. tableau 9).* Cependant, la technique de préparation étant dépendante du niveau de compétence des étudiants, le facteur préparation ne sera pas retenu dans le modèle de Cox.

Pour les succès dans le groupe AP+, les facteurs *correspondance LO et LW* et *courbure* sont étroitement liés (Chi^2 p= 0.033 ; OR= 10.286), ce qui explique que le facteur *courbure* ait été retiré du modèle de Cox final. Le niveau d'obturation correct *(p=0.002)* apparait comme un facteur prédictif primordial et reflète la nécessité de pouvoir préparer et nettoyer l'endodonte jusqu'à l'apex. La correspondance entre le niveau de préparation et le niveau d'obturation est aussi un facteur de guérison *(p=0.004).* La surobturation (obturation à l'apex avec dépassement de ciment) favorise également la cicatrisation périapicale *(p=0.02).* Pour finir, le nombre de canaux traités apparait comme facteur prédictif de la cicatrisation apicale *(p=0.004).*

3. Discussion :

3.1. Analyse des biais et répercussion sur les résultats :

La population observée n'a pas été recrutée par randomisation à partir du listing des 503 patients qui avaient bénéficié de soins endodontiques durant les années universitaires de 1999 à 2001. Le choix d'une information exhaustive des patients est motivé par un souci d'obtenir une réponse des patients à l'enquête la plus large possible (d'autant plus que la plupart de cette patientèle n'avait plus de soins en cours) et ainsi avoir une puissance raisonnable de l'analyse statistique.

Néanmoins, nous pouvons constater que la population recrutée est majoritairement féminine (2/3 de femmes pour 1/3 d'hommes) et nous pouvons avancer l'éventualité d'un biais de recrutement ; les femmes seraient vraisemblablement plus sensibilisées à la santé bucco-dentaire et à la qualité des soins prodigués. Nous avons d'ailleurs pu constater que la grande majorité des patients étaient demandeurs de soins supplémentaires et voyaient dans cette consultation de suivi l'occasion de reprendre contact avec le CSERD.

Cependant, l'homogénéité des 2 groupes a été vérifiée au niveau de la répartition selon l'âge, le sexe et les catégories socio-professionnelles.

3.2. Réponse aux questions posées :

Nous avons délibérément scindé la population cible en 2 sous-groupes pour éviter d'analyser une population hétérogène tant au niveau de la pathologie initiale que de la réponse au traitement.

Les taux de succès calculés sur ces 2 échantillons sont d'ailleurs différents : **89.2%** dans le groupe indemne de pathologie périapicale versus **67.7%** dans le groupe présentant une pathologie initiale. Ces résultats confirment ceux de la littérature qui rapporte un meilleur taux de succès sur les dents sans pathologie périapicale [19, 52, 56, 58, 59, 62, 64, 66-68, 70, 71, 106]. Cependant, nos résultats ont montrés des facteurs prédictifs de l'échec similaires dans les deux groupes : l'absence d'étanchéité coronaire et la non-correspondance entre la limite de préparation du canal et la limite de l'obturation.

De nombreux auteurs ont rapporté que l'absence d'une **restauration coronaire pérenne et adaptée** est un facteur prédictif important de l'échec thérapeutique en endodontie [83, 84, 107-111]. Nos résultats semblent le confirmer puisque de nombreuses extractions et retraitements sont liés à des lésions carieuses secondaires à un manque d'étanchéité coronaire. Nous pouvons constater néanmoins que peu d'extractions sont motivées par des pathologies périapicales évolutives ou l'absence de guérison périapicale. De ce fait, le manque d'étanchéité coronaire est probablement un facteur de confusion plus qu'un facteur prédictif réel de l'échec en endodontie [111].

Par ailleurs, nos résultats montrent que le **niveau d'obturation**, couramment utilisé comme critère de qualité de l'obturation interviendrait dans le pronostic des traitements endodontiques. En effet, un défaut d'obturation ou l'absence d'obturation au niveau de la limite de préparation endocanalaire peut favoriser le développement d'élément pathogènes préexistants et non éliminés lors de l'ampliation canalaire.

Cependant, si ce facteur est impliqué dans l'échec thérapeutique pour des patients traités pour des pathologies du périapex [34, 44, 52, 60], son implication dans l'échec du groupe AP- apparait moins évidente. Les résultats obtenus par notre modèle de Cox dans le groupe AP- indique probablement un manque de contrôle de l'asepsie pendant le

traitement des dents sans lésion initiale. La conclusion qui s'impose est que le succès de nos traitements endodontiques dépend strictement du respect des protocoles standardisés.

Dans nos modèles de survie, **la sur-obturation** apparait comme un facteur favorisant la cicatrisation périapicale. Pour de nombreux auteurs, la sur-obturation est responsable d'un délai de cicatrisation mais pas nécessairement d'un échec du traitement [106, 112, 113]. Nos traitements réalisés sur dents avec pathologie périapicale ont plutôt un meilleur pronostique lorsqu'il y a dépassement de ciment de scellement. Cette sur-obturation est finalement le garant d'une préparation jusqu'à l'apex avec obturation *ad integrum* de l'endodonte.

Pour conclure : un niveau d'obturation incorrecte (avec sous-obturation et non concordance du niveau d'obturation avec le niveau de préparation endocanalaire) est probablement un facteur de confusion dans l'échec thérapeutique, puisqu'il n'a de poids que quand il est associé à une élimination incomplète des germes qui ont colonisé l'endodonte.

D'autres facteurs ont été évalués dans cette étude notamment le **niveau de compétence** du soignant [59, 114], les **techniques de préparation** [46, 57, 65, 67, 68, 70, 71], facteurs évoqués dans d'autres études. Notre étude n'a pu conclure à l'amélioration du pronostic avec l'instrumentation Nickel Titane. Nos résultats étaient contradictoires avec la littérature puisque un fort taux d'échecs était associé avec une préparation en rotation continue. Après analyse, il s'avère que cette technique était indiquée pour des étudiants expérimentés en endodontie, lorsque la **complexité canalaire** empêchait l'utilisation de techniques de préparation conventionnelles. Nous avions ici un biais d'indication ; l'accumulation de facteurs défavorables (difficulté d'accès, lésion apicale, complexité de l'anatomie de l'endodonte..) et l'augmentation du niveau de difficulté de la technique était systématiquement associées à l'augmentation du niveau de

compétence et de technicité ; une préparation en rotation continue et/ou un étudiant de 3ème cycle universitaire était alors privilégiés. Pour cette raison, nous avons fait le choix de retirer la technique de préparation de nos modèles de Cox finaux et de proposer des stratifications sur le niveau de compétence.

3.3. De l'intérêt des résultats par rapport à ceux déjà publiés dans ce domaine :

L'utilisation de modèles d'analyse de survie permet d'obtenir une probabilité de survie dans le temps. Nous avons constaté que les deux groupes présentent des probabilités de survie différentes à 1, 2 et 3 ans, alimentant l'hypothèse que la présence de pathologie périapicale initiale est un facteur pénalisant le succès d'un traitement endodontique par rapport à celui mené sur dent indemne de pathologie initiale [19, 52, 56, 58, 59, 62, 64, 66-68, 70, 71, 106]. Si nous avons fait le choix de proposer une analyse de survie sur les 2 groupes séparément, c'est aussi parce que l'analyse proposée **répond à une réalité clinique** ; en effet, l'évaluation d'un traitement sur dent sans pathologie périapicale initiale se base sur l'apparition ou non de symptômes et d'image radioclaire signant l'échec du traitement. L'évaluation d'un traitement sur dent avec pathologie périapicale initiale s'attache, quant à elle, à la rémission de symptômes et de l'image radioclaire préexistants, c'est-à dire au succès du traitement. Nous avons donc entrepris 1) l'étude de l'échec et le calcul de la probabilité de survie au cours du temps dans le groupe AP-, 2) l'étude de la cicatrisation apicale et le calcul de la probabilité dans le temps d'obtenir une non guérison ou une cicatrisation incomplète, prenant en compte les cas incertains.

L'autre intérêt de l'analyse de survie est de pouvoir estimer le **délai nécessaire pour obtenir une cicatrisation totale ou sub-totale** des images périapicales initiales, ce que

ne peuvent faire un modèle de régression logistique ou une analyse de survie basée sur l'échec.

Notre analyse a mis en évidence un temps de cicatrisation variant de 42 semaines à 4 ans révolus. La probabilité de cicatrisation avant deux ans est de 0.23 uniquement. De même que la probabilité de survie dans le groupe AP- à deux ans est de 0.95. Ces résultats suggèrent que les délais de réévaluation préconisés [50, 99, 115] pourraient être trop courts pour pouvoir se prononcer sur la réussite ou non à long terme des thérapeutiques endocanalaires.

4. Conclusion :

Cette première cohorte répond à un certains nombres d'hypothèses et met en évidence deux groupes pathologiques bien distincts dont le pronostic diffère après traitement endocanalaire.

Bien que notre étude soit semblable à celles déjà publiées en termes de taux de réponses et de méthodologie [60, 61, 66-68, 70, 71, 91], l'aspect rétrospectif des données initiales (pré et per opératoires) limite la précision et la qualité des données recueillies. Que dire également des traitements endodontiques commencés et non achevés pour iatrogénie qui ne rentrent pas dans l'analyse du pronostic à moyen et long terme de la thérapeutique endodontique.

Afin de confirmer les résultats obtenus tout en augmentant la puissance de l'analyse, nous avons envisagé de mettre en place une seconde étude prospective avec recrutement des patients par tirage au sort.

Partie II: Article

Prognosis factors influencing the 1 to 4 years outcome of conventional root canal treatments performed in a University School of Dentistry

Soumis dans Oral Clinical Investigation

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Abstract:

Objectives: This study investigated the long-term survival and the prognostic factors of endodontic treatments performed in a University Dental School. The aim was to calculate the probabilities of success or failure according to the follow-up extent and to assess the time allowed for a complete periapical healing.

Materials and Methods: A cohort of 185 teeth were re-examined 1 to 4 years after treatment. The outcome was assessed on the basis of radiographic and clinical criteria as success, uncertain, or failure. A multivariate survival analysis using the Cox model was used to evaluate separately teeth with (AP+) and those without initial apical periodontitis (AP-) in order to highlight the predictive factors of outcome for each group.

Results: After 2 years, the appearance of an apical periodontitis remained lower than 3.5% whereas only 22.8% of periapical healed cases were notified. The significant prognosis factors are: *(i) for (AP-),* coronal leakage (p=0.002) with the higher risk of failure (RR=19.77), absence of correspondence filling length / shaping length (p=0.026), type of teeth (p=0.041), and *(ii) for (AP+),* number of root canals (p=0.00091), correspondence filling length / shaping length (p=0.017) and over-filling (p=0.09). The failed treatments in the (AP-) group and 50 % of the successful treatments in the (AP+) group were recorded during a follow-up period from 2 to 4 years.

Conclusions: This longitudinal study shows that coronal leakage is responsible of late failure cases and that periapical healing is long to achieve.

Clinical relevance: Therefore, endodontic treatments may require a follow-up for over 2 years.

Keywords :

Endodontic treatment - Root canal treatment Outcome - Longitudinal study - Multivariate Analysis - Survival Analysis - Periapical healing

Introduction

Many studies evaluate the prognosis of endodontic treatments [19]. Literature review reveals a success rate of root canal therapeutics ranging from 44% to above 90% [83, 103]. This wide range can be explained by the variations in criteria for outcome measurements, samples proportion and the composition, the study design, the length of the follow-up period, interoperator and interevaluator variability and treatment techniques [19] as well as by the practitioners' skills [103]. Systematic reviews [41, 85] and meta-analyses [81, 83, 84, 86, 87, 107, 116] were recently proposed to identify the most important factors influencing endodontic treatment outcome.

Recently, emphasis has been placed on evidence-based health care [38, 39] and only several well-controlled cohort studies are being considered as the current basis for evidence of the outcome and prognosis of initial root-canal treatment, whereas others (cross-sectional studies) are considered to generate hypotheses.

Many cross-sectional epidemiological studies have upheld the idea that the extent and the quality of root canal filling are the most important factors influencing the outcome of endodontic treatments, on the basis that the higher prevalence of apical radiolucencies has been observed on treatments with inadequate filling [21, 23-32, 34, 103] .

However, controlled longitudinal studies have shown that infected pulp and preoperative apical periodontitis are the main predictive factors [51, 58, 64-69, 71, 106] and suggested that the filling quality would only significantly affect the prognosis of teeth with initial apical periodontitis [44, 46, 56, 70] .

The principal aim of this study is to assess the outcome of conventional endodontic treatment performed in the Dental Care Center of Nantes Public Hospital, after a minimum follow-up period of one year, which is recommended in the scientific literature [53, 99, 117, 118]. A multivariate survival analysis with a Cox model is proposed to evaluate the simultaneous influence of several tooth-related and treatment-related variables on the treatment outcome: *e.g*. initial pathologic status, dental anatomy and situation, preparation or filling techniques, re-treatment, the skills of the practitioners, number of visits, filling extent and coronal restoration. Although multivariate methods (logistic regression) have been used to assess the relative effect of each technical, clinical and biological variables that scientific literature has often evoked as possible failure factors [34, 58, 60, 66-71, 74, 90, 91, 119], survival analysis has been more rarely proposed [52, 56, 59, 61, 62]. Survival methods are more appropriate to assess dynamic and time-dependant processes like the periapical healing and the appearance of an apical periodontitis.

Based on conclusions of previous controlled or clinical studies [45-47, 56, 58-60, 64-69, 74, 106], it is useful to separately assess the treatments of patients with an initial apical periodontitis and those of patients without initial periapical pathology. In this study, we managed to highlight the predictive factors influencing the 1- to 4-year outcome of conventional endodontic therapeutics (i) correlated to the failure of the treatment of teeth without initial periapical lesion, *e.g.*, the appearance of clinical and/or radiographic signs of an apical periodontitis after treatment, (ii) as well as the factors predicting the success of the treatment of teeth with initial periapical pathology, *e.g.*, the healing of a periapical lesion.

Materials and methods

Patients

During 3 years, all patients treated and re-examined at one year in the Department of Endodontics at Nantes University were proposed to participate to the study. Data collected concerned 503 patients, exhaustively informed and equally invited for re-examination after a minimum of one year. Radiographic and clinical information concerning the initial diagnosis were provided by clinical endodontic files as well as retrospective data relating to the endodontic treatment (the extent and the quality of the root canal filling), the protocol used during the treatment, and the grade of the student.

Treatments

The treatment providers were graduate students (interns) and undergraduate students (3 different grades) supervised by qualified endodontists. Endodontic treatments were performed under controlled conditions and followed a standardized protocol. Canals were cleaned and shaped using an aseptic technique and irrigated with 2.5% NaOCl. Root canal treatments were invariably achieved (i) either with stainless-steel hand file preparation and gutta-percha laterally condensation (ii) or with Rotary file preparation and a Thermafil® filling for the most experienced students.

Follow-up examination

The recall appointment consisted in an interview, a clinical and radiographic examination. Information related to the patient was carefully recorded, as well as clinical pains, swelling, apical and gingival palpation and percussion. Status and the type of coronal restoration were also evaluated.

Radiographs were performed using the long-cone technique and standardized exposure to obtain optimal quality. Two independent observers separately analyzed the radiographs that had been calibrated prior to the study as

described by Halse & Molven [120]. When disagreement occurred, a consensus was reached, according to Lambrianidis [121]. A higher percentage of agreement was found both in the interpretation of the periapical condition and the quality of the root canal seal when radiographs were simultaneously interpreted by both observers. The opinion of a third specialist was taken into account if the opinions of the two observers continued to differ.

Principal judgment criteria

In accordance with the consensus report by the European Society of Endodontology [117, 118] on quality guidelines for endodontic treatment, we chose to assess the outcome of the treatment on both clinical and radiographic criteria. The periapical index (PAI) score was used to record the radiographic periapical status [105]. A score lower than 2 (PAI<2) was considered as an absence of a periapical pathology. For teeth with an initial radiolucency, a decreasing score reflected an *in progress* healing. One-year-results of root canal therapy were classified into 3 clinical situations: success, failure or uncertain cases [53, 99].

For survival analysis requirements, 2 events were recorded: success for patients with an initial periapical lesion (AP+) and failure for patients without initial lesion (AP-) were observed during the follow-up period.

- For patients with an initial periapical lesion, success was defined as the absence of pain, swelling and other symptoms, sinus tract, loss of function and radiographic evidence of a normal periodontal ligament space or repair of periapical tissues, *e.g.* the healing of the periapical lesion. The other situations were considered as censored.
- For patients without initial periapical lesion, failure was defined as the appearance of a periapical lesion, the persistence of clinical symptoms or the presence of continuing root resorption or hypercementosis. The other situations were considered as censored.

The statistical unit is the tooth. In a multi-rooted tooth, the condition of the most severely affected root was considered.

Others criteria

For each group, the effect on the outcome of root canal therapy of various parameters was evaluated:

- tooth (localization on dental arch, number of root canals, complexity of root canal anatomy and the presence of calcification)
- practitioner's skill (the undergraduate students *versus* the interns)
- protocol (number of sessions and inter-appointment medication)

- treatment (initial root canal treatment *versus* re-treatment, preparation and filling techniques)
- coronal restoration (absent or defective *versus* adequate)
- extent of the root canal filling (flushed to 1mm to the apex, over-filling, under-filling)
- correspondence between working length and filling length
- quality of filling condensation (hermetically sealed *versus* presence of voids)
- duration of the follow-up period after endodontic success

Statistics

The analysis was performed by the SAS 9.1 software version. A descriptive statistic analysis was firstly carried out for each group (non pathological / with apical periodontitis).

A comparison between these 2 groups was then conducted in order to detect differences in the repartition of prognosis factors.

A monovariate survival analysis (Log-rank tests) was firstly performed to evaluate the association between the event (failure of endodontic treatments in the AP-, success of endodontic treatments in the AP+ group) and each factor. Then, a multivariate analysis was carried out by Cox Proportional Hazards Estimation to select the predictive factors of endodontic failure or success for the 2 different populations.

For the monovariate analyses, the alpha risk was set at 5% and 10% for the selection of variables in the Cox model.

Results were expressed as the probability of each predictive factor effect (i) in success of root canal treatments for the AP+ group and (ii) in failure of root canal treatments for the AP- group.

Results

Descriptive analysis

Out of the 503 treated patients, more than a third of this original population was lost to follow-up and excluded: 169 had moved or their address was unknown and 2 were dead. Out of the 332 patients traced, 241 were not interested or have not reply on request. 91 patients were re-examined for outcome, representing a reply rate of 91/ 332.

The mean of patient's age was 54 years old and 61.53% were females. The social and economic categories most represented were the blue-collars and intermediate professions, either pursuing an activity or retired. The average number of treatments per patient was 2.12.

Out of 185 root canal treatments, 120 included teeth without periapical pathology previous to treatment and made up about 65% of the total. The follow-up period was about 121.28 weeks (±39.24) which represents the 1- to 4-year outcome of endodontic treatment.

Comparison between the AP+ and AP- groups

The descriptive analysis (Table 1a) shows that failure occurred for 10.8% of treated teeth without initial periapical radiolucency (AP-) and for 15.4% of teeth with apical periodontitis (AP+).

No significant difference was found between the two groups for the baseline characteristics or for the repartition of prognosis factors, except for re-treatment (p=0.0006). (Table 1b)

AP- group analysis

After 2 years, the probability of appearance of a failure remains lower than 0.035 (Figure 1). The 13 failed treatments were recorded during a follow-up period from 91 to 182 weeks (nearly 2 to 4 years).

9 teeth were extracted and 5 were re-treated. Among the extracted teeth, 4 had either symptoms or apical periodontitis and were extracted on account of periodontal diseases or prosthesis plan. Besides, only 6 of the 13 failed treatments had a hermetic coronary reconstruction. It is probably for these reasons that we recorded late failures in this population.

In the monovariate analysis, the log-rank tests showed that endodontic therapy failure was associated with an incorrect filling level (p=0.025), a defective coronal restoration (p=0.0072) and an under-filling (0.02) (Table 2a). For incorrect filling level, the risk of failure was equal to 3.92 $IC_{95\%}$ [1.19-13]. For a defective coronal status, the risk of failure was equal to 7.83 $IC_{95\%}$ [1.75-35.1]. For an under-filling, the risk of failure was equal to 4.42 $IC_{95\%}$ [1.26-15.5].

The Cox model showed that correspondence between filling level and working level (p=0.026), defective coronal status (p=0.002) and the localization of teeth on dental arch (p=0.041) (Table 2b) were statistically associated with endodontic therapy failure.

AP+ group analysis

Failure probability for teeth with initial apical periodontitis was still 0.98 one year after the root canal treatment had been achieved (Figure 2). The first complete periapical healing was observed after 56 weeks. However, the probability of periapical healing increases in time: successful cases were respectively 22.8%, 67% and 88% for a follow-up period of 2, 3 and 3.5 years. The main successfull treatments were recorded during a recall period from 1 to 4 years. 50% of periapical healing occured within 128 weeks and the last healed case was observed after 219 weeks.

In the monovariate analysis, the log-rank tests showed that endodontic therapy success was associated with preparation techniques and practitionner's skill (Table 3a). Success, for rotary preparation, was 11.3 higher $IC_{95\%}$ [2.96-43.1] (p=0.00039) than for the hand file preparation. Under-graduate students had 0.26 $IC_{95\%}$ [0.09-0.71] (p=0.009) lower success than graduate students.

However, significant statistical interaction between the covariables skill and preparation techniques was observed. In consequence, the Cox model was stratified on the preparation techniques.

The number of root canal treated (p=0.00091), the correspondence between filling level and working level (p=0.017) and the over-filling were independently linked to periapical healing (Table 3b).

Discussion

Population

In this follow-up cohort, only 91 of the 503 patients who had received endodontic treatment during the 1999-2001 period were re-examined for outcome. This reply rate was usually reported by similar studies **[58, 60, 66-71]**. Nevertheless, the re-examined population was mainly female and we advanced the hypothesis proposing a recruiting bias. Women pay more attention to their dental health and the quality of treatment. However, the ranges of age and professional categories showed that the sample is representative of the population treated in the endodontic department at Nantes University.

Design

This study was exhaustive, including all treatments achieved during a defined period. The population sample was constituted on a voluntary basis from patients who agreed to come for a follow-up consultation. Therefore, there is not a bias of selection linked to a particular treatment. The aim of this study was not to compare some protocols or treatments and changeability linked to these therapeutics was considered to be a source of random variation.

The studied population was selected on a 3 years-period which is well-representative of both the clinical practice of the Endodontics Department of Nantes University and the frequency of the pulpar and periapical pathologies.

Many prognosis factors of endodontic treatment outcome had been described in the literature [19] : the complexity of root canal anatomy (canal curvature, canal calcification, number of root canals), the localization of teeth on dental arch (difficulty of access in mouth), the preparation and filling techniques, the wrong filling quality (especially the incorrect filling level, such as sub-filling, over-filling), the number of treatment sessions, the inter-appointment medication, the skills of practitioners and the incorrect coronal restoration. The preoperative periapical status appears to be one of more decisive factor for the outcome of endodontic treatment [44-47, 52, 56, 58, 59, 64, 66-68, 70, 71, 106]. On the other hand, periapical lesion is a judgement criterion for the endodontic treatment. Moreover, epidemiological studies have revealed high frequencies of apical periodontitis in conjunction with endodontically treated teeth [24, 26, 28-31, 33, 48, 90, 112, 122-125]. Most of these studies have been cross-sectional and based on a single radiological examination. This means that the apical lesion observed on treated teeth have included lesions in a state of healing as well as persisting or newly developed lesions. Such studies are less suitable for estimating the final outcome of endodontic treatment [39, 61, 66-68, 74] . The success rates reported in these studies did not provide sufficient information on the treatment prognosis and were calculated on the assumption of the independence of all these factors [61, 95]. The purpose of this cohort was to assess all these factors as covariables in a multivariate analysis and to follow the root canal treatment survival over a 1-to 4- year period using a Cox Model. Other studies have proposed multivariate statistical analyses with logistic regression [58, 60, 66-71], but only a few with survival models [52, 59, 61, 62]. Conclusions of logistic regression models based on binomial proportions of successful cases do not reflect that the success / failure rate can be variable over time. For Örstavik [53], complete healing of preoperative periapical disease required 4 years for completion, while most cases (88%) of incomplete but initiated healing were detectable after one year. Many authors recommended a longer follow-up period [44-46, 52, 59, 61, 64, 99, 126, 127]. This approach that considered as a failure the incomplete repair over 4 years was contradicted by survival analyses with longer follow-up period [55, 59, 61]. These studies had shown that the survival probability of healing continue to increase beyond the 4 years delay. Patients without definitive status can seriously lead to misinterpretation of the results [61]. We sidestepped these problems by censoring such a situation and used a statistical method of survival analysis in order to take into account the time of follow-up. Survival multivariate analysis was considered suitable for similar studies [56, 59, 61, 62, 95]. For both these

reasons and on the assumption that prognosis factors might be different according to the initial disease, the statistical analysis was conducted by dividing the population into 2 different groups: teeth with initial apical periodontitis and teeth without such initial lesion. Moreover, to assess the evolution of the healing of pre-existing periapical radiolucencies over time, we used a particular survival analysis in which the studied event is not a failure (as usually performed) but a success. Indeed, clinical assessment of endodontic outcome might explain this choice. In practice, the practitioners recorded either if an apical periodontitis appeared, or if the periapical healing was achieved, with the regression of the initial periapical lesion. In the first case, for teeth without apical periodontitis, the clinicians tried to identify the failure of the treatment; in the second case, for teeth with a pre-existing lesion, the attempted event is the success.

Statistical unit

Previous studies [24, 44, 58] have analyzed the treatment failure on each dental root, but we chose the tooth as the statistical unit as Stoll [59] and the Toronto study [66-68]. The endodontic treatment of a multi-rooted tooth is considered as a failure when a periapical lesion occurred on one of the roots. When the unit is the root, the influence of multi-rooted teeth in the sample might be overestimated. For this reason, we chose to assess the filling quality (especially the filling level and the correspondence between filling level and working level) for each tooth. However, because sub-filling and over-filling can be observed simultaneously on a multi-rooted tooth, different types of filling defect were reported for each dental root.

Published results

Our results agreed with earlier findings showing that a high rate of success is observed on teeth without apical periodontitis [19, 103]. Two years after the endodontic therapy, more than 96% of the teeth without preoperative periapical lesions were treated successfully whereas only 22.8% of initial apical periodontitis were completely healed (PAI<2, no symptom). The preoperative periapical status appeared to be decisive for the outcome of endodontic treatment [44-47, 52, 56, 58, 59, 62, 64, 66-68, 70, 71, 106]. In our study, the analysis is related to healing events and it appears that several treatments with apical periodontitis displayed no progression in their disease during re-examination. The survival curve (Fig 2) showed that healing can be achieved many years after treatment, thus increasing the difficulty of endodontic outcome analysis. These results were in agreement with previous studies [55, 61, 88] with a healing process beyond a period of 4 years. Although these teeth were functional, a recall should be conducted 4 years after the achievement of the treatment to conclude on healing success or failure [99].

Using a Cox model, we showed that coronal restoration, correspondence between filling level and localisation of teeth on dental arch were independently associated with failure in the patient group without initial periapical lesion (AP-).

In the patient group with an initial apical periodontitis (AP+), overfilling, root canal number and correspondence between shaping and filling lengths were independently associated with wound healing.

It has been argued that the endodontic outcome was intimately linked to the quality of treatment performed [103]. The debate about the effect of the filling quality has been raised by many authors [24, 26, 28-31, 33, 39, 44-46, 48, 66-68, 90, 112, 122-125, 127]. Although several multivariate analysis confirmed this hypothesis [34, 52, 56, 59], others did not find any significant effect of the filling extent on failure of root canal treatment [60, 64, 66-68, 70, 71]. Although the filling length, and especially the under-filling appeared to be significant in the monovariate analysis for teeth without initial apical periodontitis, our survival multivariate model did not identify the incorrect filling length as directly responsible for failure. In fact, the discordance of the filling level and the instrumentation level appeared to be a better prognosis indicator of endodontic failure. In this sample, we noticed that the majority of filling defects displaying a difference between filling level and instrumentation level were actually under-fillings. Many authors have shown that there is a correlation between significant under-fillings (>2mm) and the presence of periapical lesions [26, 29, 31, 127]. According to Sjögren *et al.* [44], the sub-filling is related to failure only for infected root canals. Our results suggested that undergraduate students might have committed an error in controlling the root-canal asepsis during the treatment. In the case of sub-filling, the incomplete root canal filling created vacuities that could favour the development of persistent pathogenic elements (toxin, bacteria) and could initiate a periapical pathology. The other explanation was that, because of the nature of this study, the initial pulpal diagnosis could not be retrospectively certified. Consequently, partial pulp necrosis and necrobiosis, could be integrated into the sample without periapical pathology and lack any clinical and radiological sign of periapical inflammation. Several authors have shown that pulp necrosis had a worst outcome rate than pulpitis [46, 58, 59].

Several studies have reported a higher risk of failure with an incorrect filling extent of teeth with apical periodontitis [34, 44, 52, 60] although others have concluded that the filling level exerted no significant influence on endodontic outcome [64, 66-68, 70, 71, 106]. Our Cox model reported that the correspondence of the filling level and the instrumentation level was a more significant predictive factor for the healing of a preoperative apical periodontitis compared to correct filling level.

In our models, over-filling did not appear as a failure factor. On the contrary, for the group with initial apical periodontitis, over-filling is correlated to periapical healing. For several authors, over-filling is responsible for a healing delay, but not necessarily for an endodontic failure [106, 112, 113]. Extruded filling materials, especially root canal cements may become resorbed and yet still remained in the periradicular tissues as microscopic particles. In all likelihood, the root canal filling materials are not as irritating to the periradicular tissues as microbial factors such as bacterial cell and harmful metabolic by-products [106]. Our models were in accordance with previous findings [58, 64, 66-68, 106, 128] that support that the major factors associated with endodontic failure were the persistence of bacterial infection in the canal space and/ or the periradicular area and the preoperative apical periodontitis. The apical extent of root canal treatment (i.e., flush-filled, under-filled or over-filled) is not closely related to the endodontic outcome but is probably a confounding factor. In other words, the filling extent is partly responsible of the failure when linked to an incomplete elimination of microbes in infected root-canals or with a bacterial inoculation of the periapical tissues.

In France, microbial samples were not routinely used to verify the absence of bacteria in root canal space before filling. Intracanal sampling techniques actually had limited predictive value [79, 88]. Moreover, retrospectively, it was difficult to assess the well-controlled asepsis during the treatment.

In our study, the variable skill and preparation technique was correlated to endodontic treatment outcome in our monovariate analysis performed on a group with initial apical periodontitis. This observation concerning operator's skill was contradicted by previous studies [114] [59]. Although several authors [46, 57, 65, 67, 68, 70, 71] found that root-canal therapy is technique–sensitive, the analysis of colinearity showed a strong correlation between the practitioners' grade and the techniques used in this cohort. This interaction can be explained by the fact that rotary technique was mainly used by graduate students whereas the hand file preparation technique was performed by undergraduate students. Data of the preparation techniques, as a confounding factor, were stratified in the Cox model for the group with initial apical periodontitis.

Our Cox models highlighted that posterior teeth carry a higher risk of failure for the patients without initial apical periodontitis and that periapical healing occurred more often for single-root teeth. This finding concurs with some other observations [61]. The influence of the tooth localization on the dental arch and the number of root canals have been assessed by many authors [24, 46, 47, 61, 62, 66-68, 70, 71, 76, 129] with controversial conclusions. Only few studies [61, 66-68], have reported that tooth localization and number of root canals are significant predictive factors of failure in endodontics. Our observations were consistent with these studies; i.e., the outcome differed for single-rooted and multi-rooted teeth only for teeth with preoperative apical

periodontitis, reflecting the complexity of eliminating root canal infection in the multi-rooted teeth. This also confirms the need to use of the tooth as the unit of evaluation [19, 67, 68].

Clinicians know that re-treatment is a difficult procedure which outcome largely depends on the complexity of root canal morphology and the presence of preoperative apical periodontitis. Previous studies illustrated these difficulties and demonstrated that re-treatment outcome seems to depend on alterations in the natural course of the root canals caused by initial endodontic treatment [70, 72], as well as on radiolucency [70]. Sjögren *et al.* [44] have suggested that re-treatment appears to be decisive for the outcome of endodontic treatment, but other authors did not support this hypothesis [58, 59, 126] and this tallies with our results. Moreover, some meta-analyses have reported no different estimated pooled success rates for both initial and secondary root canal treatments, as well as the same significant prognostic factors *e.g.* the presence/absence of pre-operative periapical lesion, the apical extent of root filling and the quality of coronal restoration [83, 84, 107].

The Cox model showed that the lack or imperfect coronal restoration compromised the long-term success of endodontic treatment. Many papers have also concluded that the coronal leakage might be an essential prognosis factor in endodontics [83, 84, 107-110]. Our results are in agreement with Vire [130] who concluded that tooth loss is often the direct outcome of caries revival or coronal fracture and not linked to an apical periodontitis. As suggested by Chugal *et al*. [111], the impact of the coronal leakage or the type of restoration on the endodontic outcome must be carefully analyzed in order to identify and spread any confounding factor. In this study, tooth requiring extraction was noted “failed/not healed” where as the tooth loss was independent of apical diseases.

Conclusions:

This work shows that teeth with no preoperative periapical lesion cannot be considered as a therapeutic problem, given that more than 95% of these teeth were treated successfully after 2 years. The probability of healing in the group with initial periapical lesions is lower than 23% before 2 years and this underlines the difficulty of treatment in such a situation. However, there are identifiable factors associated with the success or the failure of endodontic treatments. Our survival model shows that the discrepancy between the filling extent and the instrumentation level is a significant negative prognosis factor in endodontics success. These findings support the fact that the complete disinfection of root canal space followed by the complete root canal filling to avoid development of pathogenic elements is the core concept of the success of endodontic therapy. For teeth without an initial periapical lesion, the outcome of the treatment is also associated with the coronal restoration and with

the accessibility of the teeth. For teeth with a preoperative apical periodontitis, the number of root canals and the over-filling is also a prognosis factor.

This study has laid emphasis on the fact that periapical healing is a long and delicate process and may require a follow-up for over 4 years.

Table 1a: Root canal outcome for each population according to ESE guidelines

	Without initial apical periodontitis (AP-) n=120	With initial apical periodontitis (AP+) n=65	Difference between the 2 groups (Chi ^{2}) p value
Failure	**10.8%(**13)	**15.4%(**10)	0.370
Success	**89.2%**(107)	**67.7%**(44)	< 0.001
Uncertain cases*		**16.9%**(11)	< 0.001

Results are expressed as proportions of failure, success and uncertain cases.

**In this cohort, the uncertain cases have been assessed before the 4-year period required to conclude whether they were a success, or a failure. (Reit 1987)*

Table 1b: Baseline characteristics and repartition of prognosis factors in AP+ and AP- groups.

	AP-		*AP+*		**Chi ^{2} p-value**
	n	**%**	**n**	**%**	
Localization of teeth on dental arch					
anterior	65	54 %	44	68 %	*0.0742*
posterior	55	46 %	21	32 %	
Root canal number					
single-rooted teeth	47	39 %	34	52 %	*0.0854*
multi-rooted teeth	73	61 %	31	48 %	
Rootcanal Calcification/Obliteration					
absence	109	92 %	58	89 %	*0.5963*
presence	10	8 %	7	11 %	
Filling level					
correct	67	56 %	33	52 %	*0.5796*
incorrect	53	44 %	31	48 %	
Correspondence between filling level and working level					
correspondence	88	84 %	51	93 %	*0.1126*
discrepancy	17	16 %	4	7 %	
Re-treatment					
absence (initial treatment)	76	63 %	24	37 %	***0.0006***
presence	44	37 %	41	63 %	
Skill					
= graduate students (interns)	27	24 %	8	13 %	*0.0821*
= undergraduate students	86	76 %	54	87 %	
Inter-appointment medication					
= none	29	24 %	12	18 %	*0.6323*
= calcium hydroxyde	61	51 %	37	57 %	

= others	30	25 %	16	25 %	
Number of treatment sessions					
immediate filling	63	53 %	33	52 %	*0.9426*
〉1	56	47 %	30	48 %	
Preparation techniques					
Hand file preparation	112	93 %	61	94 %	***1***
Rotary preparation	8	7 %	4	6 %	
Restoration					
correct	101	89 %	51	84 %	*0.8667*
defective	13	11 %	10	16 %	
Root canal curvature					
absence (right root canal)	86	72 %	52	80 %	*0.2139*
significant curvature	34	28 %	13	20 %	
Over-filling					
absence	107	90 %	55	87 %	*0.5916*
presence	12	10 %	8	13 %	
Under-filling					
absence	77	65 %	40	63 %	*0.8708*
presence	42	35 %	23	37 %	

Results are expressed as proportions. Comparison of prognosis factors repartitions in AP+ and AP-groups is obtained with Chi^2 tests. Significant difference is expressed as p value ≤ 0.05.

Table 2a : Patients without initial apical periodontitis ***(AP-)***.

Monovariate analyses: Factors correlated to failure**.**

	RR	**IC(RR)$_{95\%}$**	**p-value**
Localization of teeth on dental arch			
anterior	1		
posterior	2,66	[0,86-8,20]	*0,089*
Root canal number			
single-rooted teeth	1		
multi-rooted teeth	1,77	[0,57-5,52]	*0,33*
Root canal Calcification/Obliteration			
absence	1		
presence	0,97	[0,12-7,67]	*0,97*
Filling level			
correct	1		
incorrect	3,92	[1,19-13]	***0,025***
Correspondence filling level /working level			
correspondence	1		
discrepancy	1,67	[0,44-6,38]	*0,45*
Re-treatment			
absence (initial treatment)	1		
presence	2,08	[0,65-6,62]	*0,21*
Skill			
graduate students (interns)	1		
undergraduate students	0,80	[0,22-2,97]	*0,74*
Inter-appointment medication			
none	1		
calcium hydroxyde	1,73	[0,45-6,62]	*0,43*
others	0,92	[0,15-5,56]	*0,93*

Number of treatment sessions			
immediate filling	1		
〉1	1,29	[0,43-3,85]	*0,65*
Preparation techniques			
Hand file preparation	1		
Rotary preparation	1,83	[0,23-14,3]	*0,57*
Restoration			
correct	1		
defective	7,83	[1,75-35,1]	***0,0072***
Root canal curvature			
absence (right root canal)	1		
significant curvature	0,77	[0,21-2,86]	*0,70*
Over-filling			
absence	1		
presence	0,66	[0,08-5,19]	*0,69*
Under-filling			
absence	1		
presence	4,42	[1,26-15,5]	***0,02***

Results are expressed as a relative risk (RR) with its confidence interval for each prognosis factor. Prognosis factors are separately assessed with monovariate survival analyses (Log-Rank). Significant effect on treatment outcome is expressed as p value ≤0.05.

Table 2b : Patients without periapical lesion ***(AP-)***.

Final Cox model: factors correlated to ***failure***.

	β	**S(β)**	**RR**	**IC(RR)$_{95\%}$**	**p-value**
Restoration					
correct	0		1		
defective	2.98	0.97	19.77	[2.95 – 132.7]	***0.0021***
Correspondence filling level / working level					
correspondence	0		1		
discrepancy	2.13	0.96	8.45	[1.29 – 55.4]	***0.026***
Localization of teeth on dental arch					
anterior	0		1		
posterior	1.98	0.97	7.27	[1.08 – 49.0]	***0.0410***

The « risk of failure » is 19.77 higher for teeth with a defective restoration, p=0.0021.

The « risk of failure » is 8.45 higher for teeth with a discrepancy filling level / working level, p=0.026.

The « risk of failure » is 7.27 higher for posterior teeth, p=0.041.

Table3a: Patients with initial apical periodontitis ***(AP+)***.

Monovariate analyses: factors correlated to ***success*** (healing).

	β	**S(β)**	**RR**	**IC(RR)$_{95\%}$**	**p-value**
Localization of teeth on dental arch					
anterior	0				
posterior	-0,63	0,36	0,53	[0,27-1,07]	*0,075*
Root canal number					
single-rooted teeth	0		1		
multi-rooted teeth	-0,52	0,32	0,59	[0,32-1,10]	*0,099*
Root canal Calcification/Obliteration					
absence	0		1		
presence	-0,05	0,60	0,95	[0,29-3,10]	*0,93*
Filling level					
correct	0		1		
incorrect	-0,37	0,32	0,69	[0,37-1,30]	*0,25*
Correspondence filling level / working level					
correspondence	0		1		
discrepancy	-0,56	0,57	0,74	[0,14-2,43]	*0,45*
Retreatment					
absence (initial treatment)	0		1		
presence	-0,18	0,32	0,84	[0,45-1,56]	*0,58*
Skill					
graduated student (interns)	0		1		
undergraduate students	-1,37	0,52	0,26	[0,09-0,71]	***0,009***
Inter-appointment medication					
none	0		1		
calcium hydroxyde	0,74	0,55	2,09	[0,72-6,08]	*0,18*

others	0,88	0,58	2,41	[0,77-7,56]	*0,13*

Number of treatment sessions					
immediate filling	0		1		
〉1	-0,31	0,32	0,73	[0,39-1,36]	*0,32*
Preparation techniques					
Hand file preparation	0		1		
Rotary preparation	2,42	0,68	11,3	[2,96-43,1]	***0,00039***
Restoration					
correct	0		1		
defective	-0,63	0,48	0,53	[0,21-1,37]	*0,19*
Root canal curvature					
absence (right root canal)	0		1		
significant curvature	0,42	0,42	1,51	[0,66-3,47]	*0,33*
Over-filling					
absence	0		1		
presence	-0,45	0,53	0,64	[0,23-1,80]	*0,4*
Under-filling					
absence	0		1		
presence	-0,10	0,34	0,91	[0,46-1,77]	*0,77*

Table 3b: Patients with initial apical periodontitis ***(AP+)***.

Final Cox model: factors correlated to ***success*** (healing).

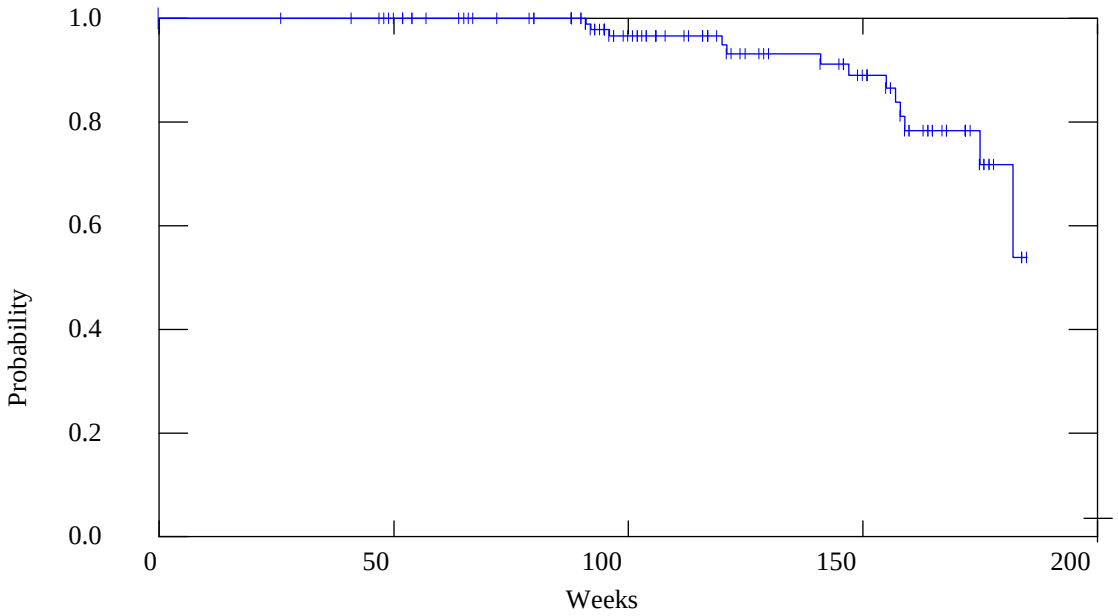
	β	**S(β)**	**RR**	**IC(RR)$_{95\%}$**	**p-value**
Over-filling					
absence	0		1		
presence	0.80	0.47	2.23	[0.88 – 5.64]	***0.09***
Root canal number					
single-rooted teeth	0		1		
multi-rooted teeth	-1.49	0.45	0.23	[0.09 – 0.55]	***0.00091***
Correspondence filling level / working level					
correspondence	0		1		
discrepancy	-2.86	1.20	0.06	[0.01 – 0.60]	***0.017***

The « risk of healing » is 2.23 higher for teeth with an over-filling, p=0.09.

The « risk of healing » is 4.35 (1/0.23) lower for multi rooted teeth, p<0.001.

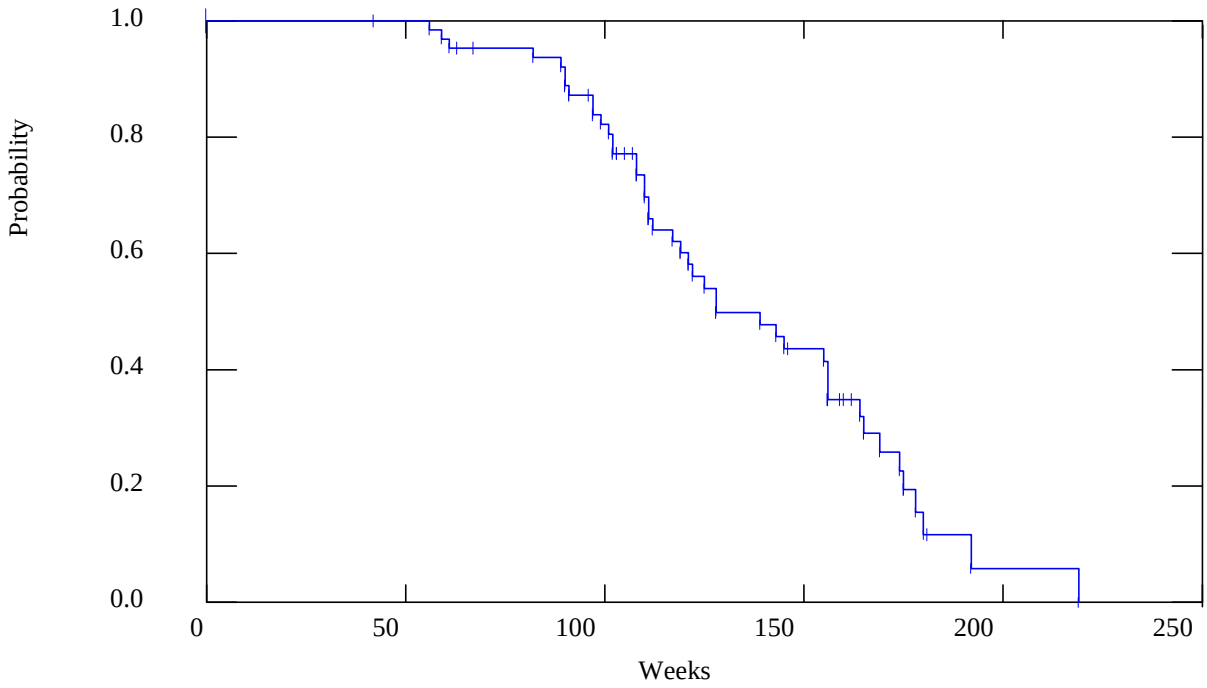
The « risk of healing » is 16.6 (1/0.06) lower for teeth with a discrepancy correspondence between filling level and working level, p=0.017.

Figure 1: Probability of success of root canal treatments for teeth without initial apical periodontitis (AP-)



Survival curve: *The probability of success decreases from 91 to 182 weeks, during which period all the failed treatments were observed.*

Figure 2: Probability of failed or incomplete periapical healing for teeth with an initial apical periodontitis (AP+)



Survival curve: *The probability of absence or incomplete healing decreases from 56 to 219 weeks, during which period all the successful treatments with a complete periapical healing were observed.*

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Partie III : Cohorte prospective

La première étude rétrospective nous a apporté plusieurs avantages :

- Estimer la proportion de succès des traitements endodontiques dont bénéficient les patients du Centre de Soins Dentaires. Ainsi, nous avons pu calculer un effectif d'échantillon suffisant pour une cohorte longitudinale prospective d'une puissance élevée.
- Mettre en évidence les failles et biais de la première évaluation pouvant entacher les conclusions finales.

Dans la première étude, la faible prévalence des techniques de préparations canalaires avec des instrumentations Nickel-Titane en rotation continue ne permettait pas d'évaluer leur impact réel sur le pronostic endodontique.

La seconde étude a été réalisée avec une période d'inclusion suffisamment longue pour bénéficier de la généralisation au cours du temps de l'utilisation de cette technique parmi la population étudiante pour pouvoir en quantifier les effets.

- Réévaluer certaines hypothèses de travail. Nous avons, entre-autre, élargi notre temps de suivi pour confirmer (ou infirmer) nos premières conclusions concernant le temps de survie des traitements et le délai de cicatrisation.

Nous avons donc envisagé **une seconde étude clinique** qui nous fournisse un bon niveau de preuves pour nos résultats finaux. Cette cohorte prospective a été construite afin d'obtenir un échantillon de traitements endocanalaires représentatifs de ceux réalisés au Centre de Soins Dentaires, ainsi qu'une puissance élevée.

1. Matériels et Méthode :

1.1. Objectifs :

Cette seconde étude est une cohorte prospective dont les objectifs restent les mêmes que ceux de l'étude précédente :

- Evaluer dans le temps le pronostique des thérapeutiques endocanalaires réalisées au Centre de Soins et de Traitements Dentaires-CHU Hôtel Dieu de Nantes, à partir d'une cohorte de patients ayant bénéficié d'un ou plusieurs traitements, au moins un an auparavant.
- Identifier les facteurs ayant un effet sur la survie à moyen et long terme de nos traitements.

1.2. Hypothèses de travail :

Nous avions plusieurs hypothèses de travail à explorer ou à confirmer :

- La proportion de réussite des traitements endodontiques réalisés au Centre de Soins Dentaires avec des protocoles standardisés et des techniques de référence excède 0,80 à un an pour une population indemne de pathologie périapicale initiale. Cette proportion diminue avec l'existence d'une pathologie périapicale au moment du traitement et selon le niveau et la qualité de l'obturation canalaire.
- Différents facteurs liés au niveau de compétence de l'intervenant (étudiants de second cycle, internes ou praticiens) aux techniques de préparation et d'obturation

endocanalaires, à la dent (difficultés d'accès, nombre de canaux) pourraient influer sur le succès de nos traitements endodontiques.

Par ailleurs, les résultats de la précédente évaluation ont soulevé d'autres points d'interrogations que nous tenterons d'élucider par ce travail :

- Quel est le temps nécessaire à la cicatrisation apicale ?
- L'évaluation à un an permet-elle d'établir un pronostic à long terme ?
- Quelle est le taux réel d'échec liés à l'iatrogénie ?

1.3. Population étudiée :

Nous avons pu recruter notre échantillon à partir de la population de patients consultant au Centre de soins dentaires pour une réhabilitation globale de la cavité buccale. Ces patients sont en général compliants et engagés dans un long processus de soins. Nous avons ainsi évité un nombre important de perdus de vue et garanti un suivi à moyen et long terme des thérapeutiques endodontiques, sans contraindre les patients à revenir pour l'évaluation.

Nous avons recruté les patients par tirage au sort jusqu'à obtenir un nombre suffisant de traitements endodontiques. Cet échantillonnage avec un grand nombre de sujets limitera les biais et permettra d'extrapoler les résultats obtenus à la population prise en charge au Centre de Soins Dentaires (CSERD) de Nantes.

118 patients ayant bénéficié d'une ou plusieurs thérapeutiques endodontiques ont été recrutés pour cette étude. Ces patients ont été informés et ont pu bénéficier de plusieurs examens de contrôle lors de leur prise en charge globale jusqu'à achèvement de leur soins bucco-dentaires et prothétiques. Ce recrutement s'est fait sur plusieurs années.

1.4. Critères d'évaluation :

Les données concernant la pathologie initiale, le traitement endodontique et le suivi clinique ont été consignées sur un formulaire de recueil élaboré à cet effet *(cf. annexe).* Le recueil prospectif nous a permis d'obtenir des informations sur l'indication de traitement (pathologie aigue ou chronique, indication prothétique…), sur la morbidité liée aux aléas thérapeutiques et l'iatrogénie, ainsi que sur les motifs d'échecs (endodontiques et autres).

L'évaluation de la thérapeutique pourra être répétée plusieurs fois, selon la disponibilité des investigateurs et les rendez-vous des patients au CSERD.

1.4.1. Critère principal : Succès/Echec [53, 99] :

L'évaluation clinique et radiologique de l'endodontie à 1 an minimum après réalisation du traitement endodontique s'appuie sur les critères définis ci-dessous (*cf. tableau 1*).

L'évaluation radiographique se fait à partir de clichés rétroalvéolaires réalisés en incidence orthocentrée. Sont observés la présence ou non d'épaississement ligamentaire, la présence et le volume d'image radioclaire périapicale. Conformément à la littérature dans ce domaine [74, 77], le PAI (Periapical Index Score System) [105] est utilisé également dans l'évaluation.

1.4.2. Critères secondaires :

Les facteurs étudiés sont semblables à ceux de la première étude et sont ceux décrits dans la littérature [58, 66, 131].

Population indemne de pathologie périapicale initiale	*Population avec pathologie périapicale initiale*
Echec : -Apparition de signes cliniques tels que des douleurs provoquées ou spontanées, une fistule, une voussure vestibulaire ou palatine révélant une pathologie d'origine endodontique -Apparition de signes radiologiques avec PAI≥ 2 -Dent non fonctionnelle ou extraite	**Echec** : non rémission d'une pathologie périapicale préexistante. -Apparition de signes cliniques tels que des douleurs provoquées ou spontanées, une fistule, une voussure vestibulaire ou palatine révélant une pathologie d'origine endodontique -Augmentation du volume de l'image radioclaire avec augmentation de l'indice PAI. -Dent non fonctionnelle ou extraite
Succès : -Absence de signes cliniques et radiologiques avec un PAI≤ 1 [105] -Dent fonctionnelle	**Succès** : -Absence de signes cliniques -Disparition totale de l'image radioclaire de la lésion apicale avec PAI≤ 1 [105], signant une cicatrisation périapicale complète ou subtotale. - Dent fonctionnelle
Cas incertain : -Signes cliniques inconstants, de faible intensité et intermittents dont l'origine n'est pas clairement déterminée (origine endodontique non prouvée)	***Cas incertain :*** -Signes cliniques inconstants, de faible intensité et intermittents - Non régression notable de l'image periapicale radioclaire

***Tableau 1** : Critères d'évaluation clinique et radiographique des thérapeutiques endodontiques.*

1.5. Analyse statistique :

1.5.1. Nombre de sujets :

Il s'agit d'une cohorte prospective. Le mode de calcul ne se fait pas de la même façon que Trope et al [77], car ce n'est pas une étude de comparaison de survie des dents traitées sans pathologie périapicale initiale avec celle des dents avec pathologie avant traitement. Le nombre de sujets nécessaires est calculé à partir de l'intervalle de confiance défini avec un risque α à 0.05.

Nous avons considéré que 250 dents traitées produiraient une analyse avec une puissance importante.

1.5.2. Evénement attendu et événements censurés

1.5.2.1. Population indemne de pathologie périapicale :

Comme pour l'étude précédente, l'échec est l'évènement observé pour l'analyse de survie des dents traitées endodontiquement.

Les événements censurés (à droite) seront les succès thérapeutiques et les cas incertains.

Pour la cohorte prospective, lorsque nous avons observé un succès thérapeutique dans le groupe sans pathologie périapicale initiale, nous avons décidé d'arrêter la date de point à l'évaluation réalisée à un an ou proche d'un an. La majorité des succès ont été suivi au long cours, bien au-delà de l'année préconisée dans les recommandations ; pour éviter de surestimer le délai de survenue du succès, nous avons donc enregistré le succès à un an, l'état restant inchangé par la suite.

En cas d'évaluation précoce (avant un an) sans échec, le sujet est noté incertain jusqu'à la prochaine évaluation.

1.5.2.2. Population avec pathologie initiale :

Dans un premier temps, l'évènement attendu sera l'échec et les évènements censurés seront les cas incertains et les succès.

Il nous semble également intéressant de suivre dans le temps la régression des images radiographiques de pathologie périapicale jusqu'à cicatrisation complète. C'est pourquoi, dans ce groupe, une deuxième analyse sera réalisée avec le succès comme évènement attendu (cicatrisation complète ou subtotale) et les cas incertains et échecs thérapeutiques comme évènements censurés.

1.5.3. Estimation :

Estimations ponctuelles au moyen de pourcentages, moyennes et écart-types pour les variables qualitatives et quantitatives.

1.5.4. Analyse univariée:

Les analyses consisteront à tester l'existence d'une relation entre les variables étudiées prises séparément et la réussite ou l'échec du traitement endocanalaire au moyen d'un Log Rank.

1.5.5. Analyse multivariée :

Les facteurs qui auront été précédemment identifiés dans les analyses univariées comme liés à la réussite ou à l'échec du traitement endocanalaire avec un seuil de signification à $p<0.20$, seront ensuite incorporés dans un modèle de Cox.

L’utilisation de méthodes de sélection pas à pas ascendantes ou descendantes dans l’analyse multivariée permettra de sélectionner les facteurs pronostiques des thérapeutiques endodontiques avec un seuil de signification à $p<0.05$.

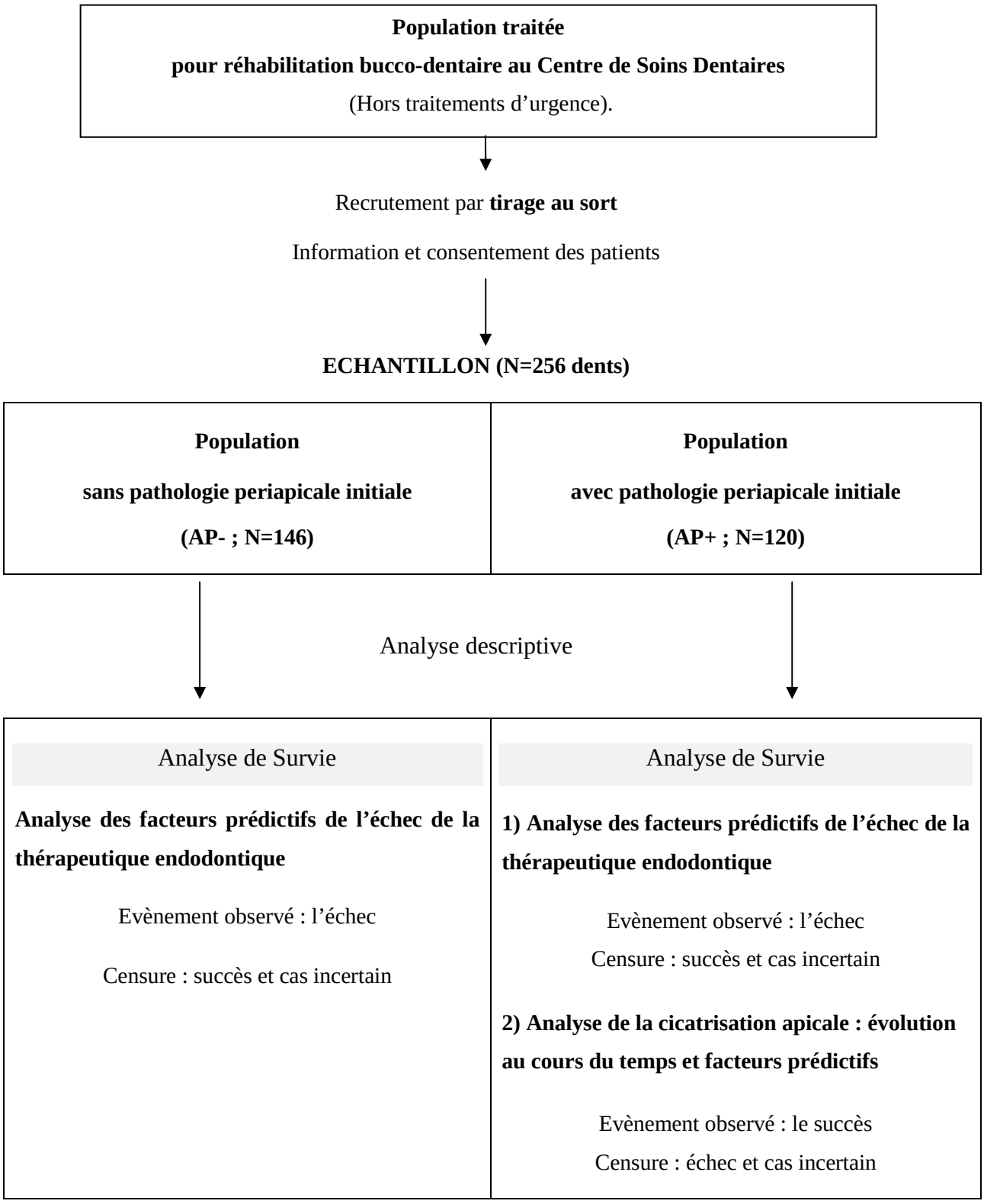


Figure 1 : *Méthodologie de la cohorte prospective.*

2. Résultats :

2.1. Analyse descriptive :

2.1.1. Résultats thérapeutiques :

Nous avons donc obtenu un échantillon de **107 patients**, ce qui représente un total de **256 traitements** endodontiques (2.39 dents traitées par patients) dont **146 r**éalisés sur dents sans pathologie périapicale (groupe AP-) et **110** sur dents avec pathologie périapicale (groupe AP+). La population recrutée semble représentative de celle du Centre de Soins Dentaires pour réhabilitation globale de la cavité buccale ; l'âge moyen est de 55ans (± 16.23) avec une proportion équivalente d'hommes et femmes (52.3% d'hommes et 47.7% de femmes).***Tableau 2a****: Moyenne et dispersion des variables quantitatives concernant* ***le suivi des traitements*** *dans les 2 groupes :*

		AP-	AP+
Temps de suivi en mois			
	N	146	110
	Minimum	0(*)	0(*)
	Maximum	171	138
	Moyenne	24.5	27
	Médiane	34.2	18.5
	Ecart-type	31.7	26.56
Nombre de consultations de suivi			
	N	146	110
	Minimum	0	0
	Maximum	6	5
	Moyenne	2.185	1.9
	Médiane	2	2
	Ecart-type	1.083	0.888

TEST de LILLIEFORS non significatif : variables quantitatives normales

La période de suivi moyenne est **de 34.5 ± 31.7 mois** pour les dents sans pathologie périapicale initiale (AP-) **et de 27 ± 26.56 mois** pour les dents avec lésion périapicale initiale (AP+), ce qui représente une période d'observation moyenne de 1 à 5 ans pour l'ensemble de la population. Le délai de réévaluation des traitements endodontiques s'échelonne de 0 à 171 mois avec un nombre de suivis allant de 0 (iatrogénie avec échec immédiat) à 6 consultations de réévaluation. *(cf. tableau 2a)*

***Table 2b**: Résultats thérapeutiques observés au terme de l'étude clinique (juillet 2011) et répartition des causes d'échec et retraitement (en fréquences et pourcentages).*

	AP- *N=146*		*AP+* *N= 110*		***Chi²p-value***	*Population Totale* *N=256*	
	n	***%***	***n***	***%***		***n***	***%***
Evolution au terme de l'étude							
succès	*105*	*71.9*	*46*	*41.8*		*151*	*59*
cas incertains	*7*	*4.8*	*21*	*19.1*		*28*	*10.9*
échecs	*34*	*23.3*	*43*	*39.1*	***<0.001***	*77*	*30.1*
Décision thérapeutique							
abstention	*108*	*74*	*65*	*59.1*		*173*	*67.6*
retraitement	*10*	*6.8*	*8*	*7.3*		*18*	*7*
extraction	*28*	*19.2*	*37*	*33.6*	***0.027***	*65*	*25.4*
Causes d'échec et retraitement							
perte de substance par carie	*13*	*31.7*	*9*	*20*		*22*	*25.6*
iatrogénie	*7*	*17.1*	*4*	*8.9*		*11*	*12.8*
pathologie périapicale	*8*	*19.5*	*15*	*33.3*		*23*	*26.8*
lésion endo-parodontale			*5*	*11.1*		*5*	*5.8*
fracture radiculaire	*2*	*4.9*	*3*	*6.7*		*5*	*5.8*
pathologie parodontale	*3*	*7.3*	***5***	*11.1*		*8*	*9.3*
indication prothétique	*3*	*7.3*	*2*	*4.45*		*5*	*5.8*
non renseignée	*5*	*12.2*	*2*	*4.45*	*0.152*	*7*	*8.1*

Au terme de l'étude, le succès thérapeutique est observé pour **71.9**% des dents traitées sans pathologie périapicale initiale contre **41.8%** des dents avec pathologie périapicale. Le succès est nettement plus faible que celui annoncé dans la précédente étude. Dans le groupe AP+, 21 cas sont incertains et dans le groupe AP-, nous avons indiqué 7 cas incertains pour des évaluations réalisées avant un an.

Concernant l'échec thérapeutique, il représente **23%** du groupe AP- contre **39%** du groupe AP+. Ces résultats mettent en évidence la différence de pronostique entre les 2 groupes (Chi^2, $p<0.001$). **19.18%** des dents du groupe AP- sont extraites et **6.85%** sont retraitées contre respectivement **33.6** et **7.27%** dans le groupe AP+. Parmi les causes d'échecs et de retraitement dans la population globale, la pathologie périapicale vient en tête avec **26.7%** des échecs recensés, puis la perte de substance par carie secondaire avec **25.6%**.

Lorsque nous regardons les raisons de l'échec dans chaque groupe, il apparait des différences ; pour le groupe AP-, les lésions carieuses secondaires sont la première cause (31.7%), largement devant la pathologie périapicale (19.5%) et les gestes iatrogènes (17%). Pour le groupe AP+, 1/3 d'échecs est liée au développement de la pathologie périapicale *(cf. tableau 2b).*

2.1.2. Facteurs prédictifs étudiés :

***Table 3a**: Répartition des facteurs pronostiques étudiés (en fréquences et pourcentages).*

	AP- N=146		AP+ N= 110		Chi² p-value	Population totale N=256	
	n	**%**	**n**	**%**		**n**	**%**
Facteurs liés à la dent traitée							
Localisation							
maxillaire	*74*	*51 %*	*67*	*61 %*		*145*	*55 %*
mandibule	*71*	*49 %*	*43*	*39 %*	*0.189*	*115*	*46 %*
antérieure	*49*	*34 %*	*45*	*41 %*		*109*	*59 %*
postérieure	*97*	*66 %*	*55*	*59 %*	*0.227*	*76*	*41 %*
Type de dent							
monoradiculée	*76*	*52 %*	*55*	*50 %*		*131*	*51 %*
pluriradiculée	*70*	*48 %*	*55*	*50 %*	*0.745*	*125*	*49 %*
Complexité anatomique							
absence	*108*	*74 %*	*83*	*75 %*		*191*	*75 %*
présence	*38*	*26 %*	*27*	*25 %*	*0.787*	*65*	*25%*
Calcification/Obstacle canalaire							
absence	*122*	*84 %*	*91*	*83 %*		*213*	*83 %*
présence	*24*	*16 %*	*19*	*17 %*	*0.860*	*43*	*17%*
Courbure canalaire							
absente ou faible	*136*	*93 %*	*107*	*97 %*		*243*	*95 %*
courbure significative	*10*	*7 %*	*3*	*3 %*	*0.137*	*13*	*5 %*

2

	AP- N=146		AP+ N= 110		Chi² p-value	Population N=256	totale
	n	**%**	**n**	**%**		**n**	**%**
Facteurs liés à la pathologie initiale							
Pathologie aigue							
absence	*83*	*57 %*	*85*	*77 %*		*252*	*98 %*
presence	*63*	*43 %*	*25*	*23 %*	***0.001***	*4*	*2 %*
Lésion périapicale							
absence	*146*	*100 %*	*54*	*49 %*		*200*	*78 %*
présence	*0*	*0 %*	*56*	*51 %*	***0.001***	*56*	*22 %*
Volume de la lésion périapicale							
≤ 1mm			*25*	*45 %*			*10 %*
1 <v≤ 3mm			*22*	*39 %*			*9 %*
3 <v≤ 5mm			*3*	*5 %*			*1 %*
> 5mm			*6*	*11 %*	***<0.001***		*2 %*
Pathologie traumatique							
absence	*144*	*99 %*	*108*	*98 %*		*252*	*98 %*
presence	*2*	*1 %*	*2*	*2 %*	*0.775*	*4*	*2 %*
Lésion endo-parodontale							
absence	*146*	*100 %*	*106*	*96 %*		*154*	*60 %*
présence	*0*	*0 %*	*4*	*4 %*	***0.020***	*102*	*40 %*
Facteurs liés aux intervenants							
Niveau de compétence							
praticiens	*3*	*2 %*	*6*	*6 %*		*9*	*3%*
internes et étudiants de 3ème cycle	*29*	*23 %*	*21*	*21 %*		*50*	*20%*
étudiants de 2nd cycle	*98*	*75 %*	*74*	*73 %*	*0.364*	*172*	*67 %*
non renseigné						*25*	*10%*

	AP- N=146		AP+ N= 110		Chi² p-value	Population totale N=256	
	n	**%**	**n**	**%**		**n**	**%**
Facteurs liés au traitement							
Re-traitement							
non (traitement initial)	*108*	*74 %*	*46*	*42 %*		*154*	*60 %*
oui	*38*	*26 %*	*64*	*58 %*	***<0.001***	*102*	*40 %*
Indication prothétique							
non	*92*	*63 %*	*96*	*87 %*		*154*	*60 %*
oui	*54*	*37 %*	*14*	*13 %*	***<0.001***	*102*	*40 %*
Niveau d'obturation							
correct	*110*	*79 %*	*64*	*63 %*		*174*	*68%*
incorrect ou absent	*30*	*31 %*	*37*	*37 %*	***0.009***	*67*	*32 %*
Correspondance entre longueur de travail et longueur d'obturation							
correct	*134*	*97%*	*89*	*88 %*		*223*	*87.5 %*
incorrect	*4*	*3 %*	*12*	*12 %*	***0.006***	*16*	*6 %*
Sur-obturation (apex anatomique ou au delà)							
absente ou non renseigné	*150*	*97 %*	*97*	*95 %*		*247*	*96.5 %*
présente	*4*	*3 %*	*5*	*5 %*	***0.044***	*9*	*3.5%*
Sous-obturation (≥ 2 mm en deçà de l'apex)							
absente ou non renseigné	*127*	*83 %*	*74*	*72 %*		*201*	*79%*
présente	*26*	*17 %*	*29*	*28 %*	***0.044***	*55*	*21 %*

	AP- N=146		AP+ N= 110		Chi² p-value	Population totale N=256	
	n	**%**	**n**	**%**		**n**	**%**
Iatrogénie							
absence	*135*	*92 %*	*95*	*86 %*		*230*	*90 %*
présence	*11*	*8 %*	*15*	*14 %*	*0.110*	*26*	*10 %*
Médication							
aucune	*47*	*32 %*	*21*	*19 %*		*68*	*27 %*
hydroxyde de calcium	*93*	*64%*	*87*	*79 %*		*180*	*70 %*
autre	*6*	*4 %*	*2*	*2 %*	***0.026***	*8*	*3 %*
Nombre de séances de traitement							
obturation immédiate	*51*	*35%*	*24*	*22 %*		*75*	*29 %*
) 1	*95*	*65 %*	*86*	*88 %*	***0.022***	*181*	*71 %*
Technique de préparation canalaire							
préparation manuelle	*66*	*47 %*	*54*	*52 %*		*120*	*49 %*
rotation continue	*75*	*53 %*	*49*	*48 %*	*0.386*	*124*	*51 %*
Technique d'obturation canalaire							
condensation latérale	*125*	*90 %*	*89*	*90 %*		*232*	*91 %*
gutta chaude	*14*	*10 %*	*10*	*10 %*	*0.994*	*24*	*9 %*
Facteurs lies à l'étanchéité coronaire							
Restauration coronaire							
correcte	*125*	*90 %*	*90*	*88 %*		*215*	*83 %*
défectueuse ou absente	*13*	*11 %*	*12*	*12 %*	*0.964*	*45*	*17 %*
Type de restauration coronaire							
définitive	*114*	*82 %*	*77*	*77 %*		*191*	*80 %*
provisoire	*25*	*18 %*	*24*	*24%*	*0.273*	*49*	*20 %*

***Tableau 3b**: Répartition des facteurs liés à l'iatrogénie (en fréquences et pourcentages).*

	AP- *N=146*		*AP+* *N= 110*		***Chi²*** ***p-value***	*Population totale* *N=256*	
	n	***%***	***n***	***%***		***n***	***%***
Perforation							
absence	*140*	*96 %*	*108*	*98 %*		*248*	*97 %*
présence	*6*	*4 %*	*2*	*2 %*	*0.887*	*8*	*3 %*
Fêlure radiculaire							
absence	*146*	*100 %*	*109*	*99 %*		*255*	*99 %*
présence	*0*	*0 %*	*1*	*1%*	*0.278*	*1*	*1%*
Faux canal							
absence	*144*	*99 %*	*105*	*95 %*	*0.748*	*249*	*97 %*
présence	*2*	*1 %*	*5*	*5%*		*7*	*3 %*
Débris instrumental							
absence	*145*	*99 %*	*106*	*96 %*		*251*	*98 %*
présence	*1*	*1 %*	*4*	*4%*	*0.218*	*5*	*2 %*
Butée							
absence	*144*	*99 %*	***107***	***97 %***		*251*	*98 %*
présence	*2*	*1 %*	*3*	*3 %*	*0.748*	*5*	*2 %*

Les 2 groupes AP- et AP+ présentent des caractéristiques similaires, sans différence statistiquement significative en ce qui concerne la situation et les caractéristiques des dents traitées, le niveau de compétence des soignants, l'étanchéité coronaire et l'iatrogénie *(cf. tableaux 3a et 3b).* Contrairement à la première étude où l'utilisation de la préparation manuelle et l'obturation par condensation latérale étaient largement majoritaires, nous n'avons pas observé ici de différence entre les 2 groupes pour les techniques de

préparation et d'obturation utilisées : la moitié des dents a été préparée manuellement, l'autre en rotation continue. Dans les 2 groupes, l'obturation par condensation latérale reste largement majoritaire (90% des traitements).

Par contre, des différences significatives sont observées sur l'état pathologique initial, naturellement, mais aussi sur des facteurs liés au traitement, notamment **le retraitement** ($p<0.001$), **l'indication prothétique** du traitement ($p<0.001$), le **niveau d'obturation** ($p=0.009$) et la **correspondance entre niveau d'obturation et longueur de préparation** ($p=0.006$), la **présence de sur-obturation** ($p=0.044$) et de **sous-obturation** ($p=0.044$), le **nombre de séances** de traitement ($p=0.022$) et la **médication** en inter-séance ($p=0.026$).

En effet, **58%** des dents du groupe AP+ ont été retraitées contre 26% dans l'autre groupe ($p<0.001$).

37% des dents du groupe AP- ont été traitées pour raison prothétique, sans symptômes préalables, contre 13% dans l'autre groupe ($p<0.001$).

79% des dents du groupe AP- ont un niveau d'obturation correct contre 63% en AP+ ($p=0.009$).

12% des dents traitées du groupe AP+ n'ont pas des longueurs de préparation et d'obturation concordants. Dans le groupe AP-, seulement 3% des traitements sont dans ce cas ($p=0.006$).

La sur-obturation est observée pour 3% des dents AP- contre **5%** des dents AP+ ($p=0.044$).

La sous-obturation se rencontre dans **28%** des dents AP+ contre 17% des dents AP- ($p=0.044$).

35% des dents AP- ont bénéficié d'une obturation immédiate contre 22% des dents AP+ ($p=0.022$).

2.2. Analyse de survie :

2.2.1. Estimation des durées et des probabilités de survie :

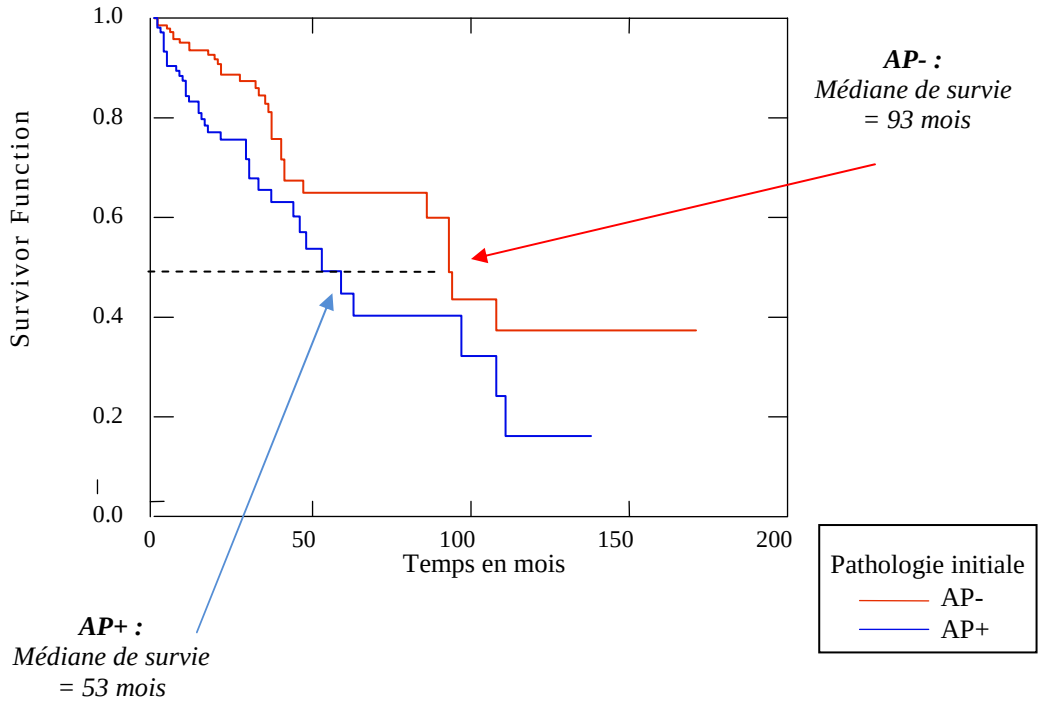
2.2.1.1. L'échec thérapeutique :

2.2.1.1.1. Population totale :

249 sujets sont retenus pour l'analyse, 7 ayant été retirés pour avoir un temps de suivi égal à 0 mois. 70 échecs ont été enregistrés et 179 observations censurées à droite. Afin d'avoir une vue d'ensemble concernant la survie des traitements endodontiques, nous avons réalisé un graphique avec les courbes de survie des traitements en fonction de la pathologie initiale *(cf.graphique 1)*,

Survenue de l'échec thérapeutique dans le temps :

Calcul de la probabilité de survie de dents traitées en fonction de la pathologie initiale.



Test du Log-rank: p=0.003

***Graphique 1**: Courbes de survie des groupes (AP-) et (AP+).*

La survie des 2 groupes est significativement différentes (p=0.003) et justifie une analyse en sous-groupes des dents traitées endodontiquement en fonction de la pathologie initiale.

Groupe AP- N = 144	Groupe AP+ N = 105
Nombre d'échecs = *32* Médiane de survie = *93 mois* Quantiles : *76% à 37 mois* *37% à 108 mois*	Nombre d'échecs = *38* Médiane de survie = *53 mois* Quantiles : *76% à 21 mois* *24% à 108 mois*

***Tableau 4:** Médianes et quantiles de survie des traitements endodontiques en fonction de la pathologie initiale.*

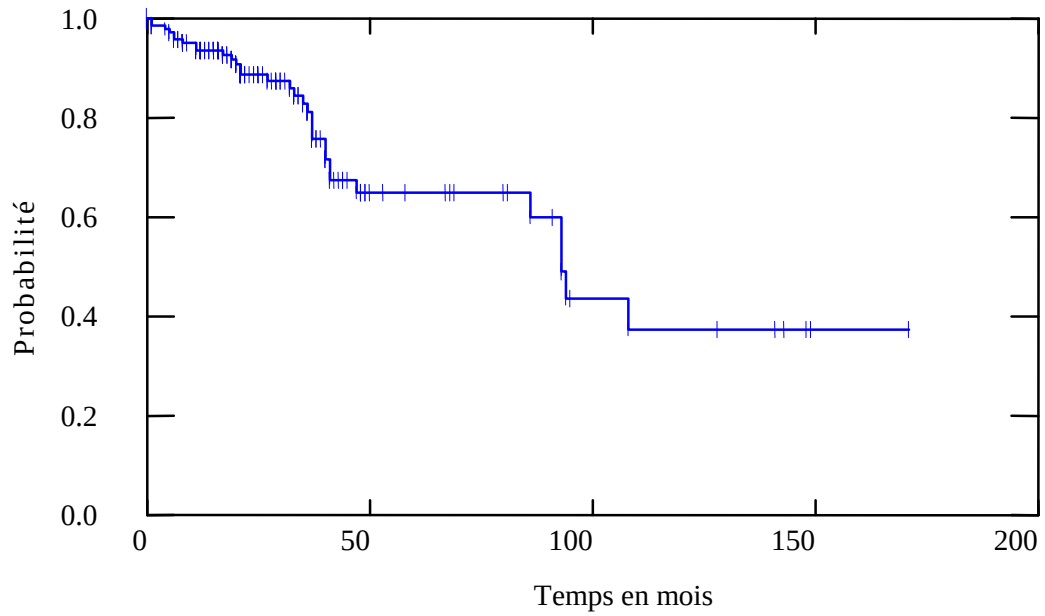
La survenue de l'échec thérapeutique semble plus précoce dans la population avec pathologie périapicale (groupe AP+) puisque la probabilité de survie est de 0.76 (76%) à 21 mois dans ce groupe contre 37 mois dans le groupe (AP-) *(cf. tableau 4).* La probabilité de survie est de 49% pour le groupe (AP+) à 53 mois contre 93 mois pour le groupe (AP-), soit plus de 3 ans plus tard. A 108 mois, la probabilité de survie n'est plus que de 24% dans la population avec pathologie périapicale initiale (AP+) contre 37 % dans le groupe sans pathologie initiale (AP-).

2.2.1.1.2. Population sans pathologie périapicale avant traitement (AP-):

La courbe de survie *(cf. graphique 2)* pour le traitement endodontique des dents sans pathologie périapicale initiale. (AP-) porte sur 144 traitements, 2 traitements étant retirés de l'analyse pour un temps de survie à 0 mois.

Survenue de l'échec thérapeutique

Calcul de la probabilité de survie des dents traitées sans pathologie périapicale initiale (AP-).



Graphique 2 : *Courbe de survie des dents traitées sans pathologie périapicale initiale (AP-).*

L*a probabilité de survie décroit de 0 à 108 mois, période pendant laquelle tous les échecs sont observés.*

L'analyse montre que les échecs sont survenus **entre 0 et 108 mois** (9 ans) après traitement. A un an (11 mois), la probabilité de survie est de 0.936 et décroit à 0.874 à 2 ans (27 mois), ce qui signifie qu'à cette période, seuls 12.6% des échecs se sont produits. La médiane de survie, temps durant lequel la moitié des échecs sont observés, est à **93 mois** (presque 8 ans). La probabilité de survie à 108 mois est de 0.374.

Causes d'échec et de retraitement	N = 36	Temps de survie MOYEN ***(en mois)***	Temps de survie MINIMUM ***(en mois)***	Temps de survie MAXIMUM ***(en mois)***	Probabilité de survie exprimée en Quantiles	
Lésion carieuse	*13*	*32*	*6*	*93*	*77%* *54%* *23%*	*19 mois* *27 mois* *37 mois*
Pathologie périapicale	*8*	*34*	*1*	*94*	*75%* *50%* *25%*	*8 mois* *17 mois* *36 mois*
Iatrogénie	*5*	*19*	*1*	*47*	*80%* *40%* *20%*	*1 mois* *6 mois* *37 mois*
Pathologie parodontale	*3*	*88*	*12*	*108*	*67%* *0%*	*12 mois* *108 mois*
Indication prothétique *(plan de traitement)*	*3*	*35*	*5*	*50*	*67%* *33%*	*5 mois* *49 mois*
Fracture radiculaire	*2*	*40*	*40*	*40*	*0%*	*40 mois*

Tableau 5 : *Causes des échecs thérapeutiques dans le groupe des dents traitées indemnes de pathologie périapicale initiale (AP-) Fréquences, moyennes et quantiles de survie.*

Les **causes d'échecs tardifs** *(cf. tableau 5)* sont essentiellement les caries secondaires par perte d'étanchéité coronaire : 8 échecs sur 13 arrivent entre 27 à 93 mois. L'autre cause invoquée est parodontale (à 108 mois).

Les **échecs précoces** sont liés à l'iatrogénie (5/7 échecs dans les 6 premiers mois) et à l'apparition d'une pathologie périapicale (6/8 échecs d'étiologie endodontique lors des 3 premières années).

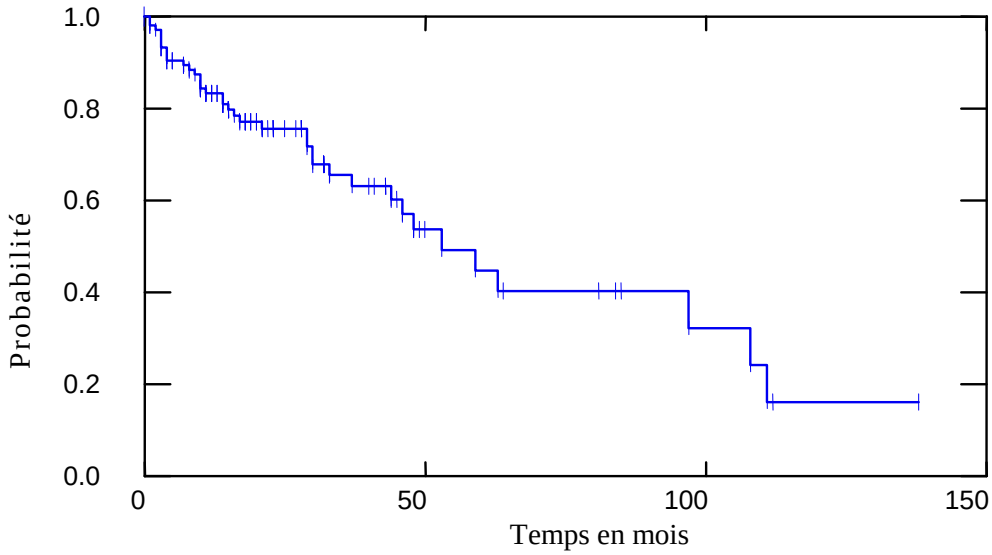
A noter cependant, **entre 3 et 4 ans** après traitement, 2 échecs pour fracture radiculaires et 2 autres associés à des perforations du plancher caméral.

2.2.1.1.3. Population avec pathologie périapicale avant traitement (AP+) :

105 sujets ont été retenus pour l'analyse, 5 ayant été retirés pour avoir un temps de survie égale 0 mois.

Survenue de l'échec thérapeutique

Calcul de la probabilité de survie des dents traitées avec pathologie périapicale initiale (AP+).



Graphique 3: *courbe de survie des dents traitées sans pathologie périapicale initiale (AP-).*

La probabilité de survie décroit de 0 à 111 semaines, période pendant laquelle tous les échecs sont observés.

Dans ce groupe, les échecs ont été rapportés **entre 0 et 111mois** (un peu plus de 9 ans). *(cf. graphique 3).*

A 1an (14 mois), la probabilité de survie est encore de 0.809 avec 19 échecs. A 2 ans (21 mois), elle est de 0.756. Un quart des échecs se produit avant 21 mois. La médiane de survie est à **53 mois**. A 108 mois, la probabilité d'échec est encore de 0.242.

Causes d'échec et de retraitement	N = 36	Temps de survie MOYEN *(en mois)*	Temps de survie MINIMUM *(en mois)*	Temps de survie MAXIMUM *(en mois)*	Probabilité de survie exprimée en quantiles	
Lésion carieuse	*9*	*33.8*	*3*	*97*	*78%* *44%* *22%*	*15 mois* *30 mois* *37 mois*
Pathologie périapicale	*13*	*19.9*	*1*	*59*	*69%* *54%* *23%*	*3 mois* *11 mois* *30 mois*
Iatrogénie	*2*	*3.5*	*2*	*2*	*50%*	*3 mois*
Pathologie endo-parodontale	*5*	*58*	*4*	*111*	*80%* *60%* *30%*	*4 mois* *29 mois* *63 mois*
Pathologie parodontale	*5*	*49.2*	*1*	*108*	*80%* *40%*	*1 mois* *21 mois*
Indication prothétique *(plan de traitement)*	*2*	*8.5*	*7*	*10*	*50%*	*7 mois*
Fracture radiculaire	*2*	*6.5*	*4*	*9*	*50%*	*4 mois*

Tableau 6: *Causes des échecs thérapeutiques dans le groupe des dents traitées avec pathologie périapicale initiale (AP+) Fréquences, moyennes et quantiles de survie.*

Les **causes d'échecs tardifs** *(cf. tableau 6)* sont essentiellement les caries secondaires par perte d'étanchéité coronaire : 6 échecs sur 9 arrivent entre 24 à 97 mois. Les autres causes sont les pathologies parodontales (à 108 mois) et endo-parodontales (à 29, 63 et 111 mois).

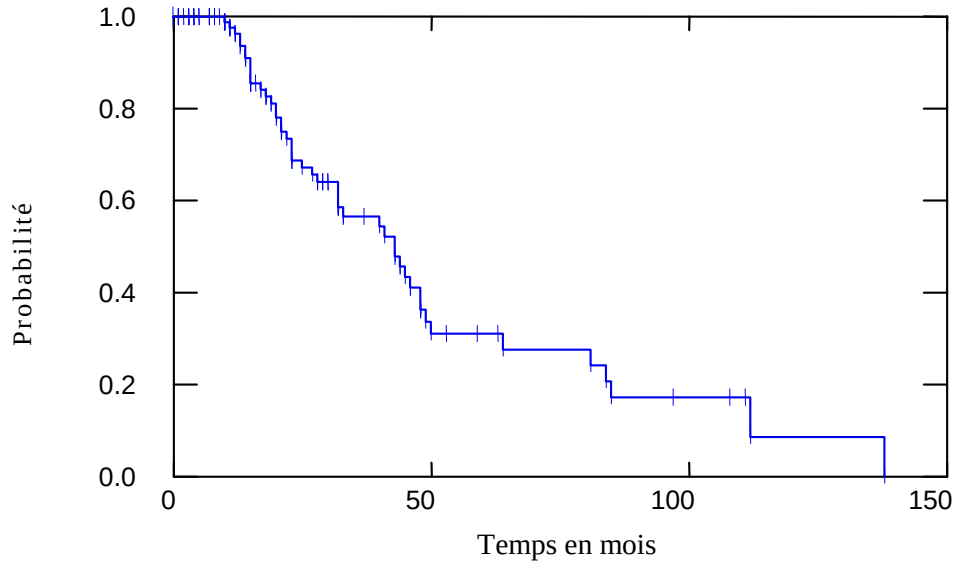
Les **échecs précoces** sont liés à l'iatrogénie (4 échecs avant 5 mois) et au développement de la lésion périapicale (plus de la moitié des échecs d'étiologie endodontique lors de la première année, le dernier observé à 48 mois).

2.2.1.2. La cicatrisation périapicale :

Pour la réalisation de l'analyse des données de survie, l'événement attendu dans ce cas précis est le **succès** et le « non-événement » regroupe les échecs et cas incertains.

Survenue de la cicatrisation périapicale complète

Calcul de la probabilité d'échec ou de cicatrisation incomplète des dents traitées avec pathologie périapicale initiale (AP+)



Graphique 4: Courbe de survenue de la cicatrisation périapicale.

La probabilité d'absence de cicatrisation ou de cicatrisation périapicale incomplète décroit de 10 à 138 mois, période durant laquelle tous les succès avec disparition totale de l'image radioclaire sont observés.

La cicatrisation périapicale s'achève avec un délai très variable, puisqu'elle peut être constatée en quelques mois ou peut se prolonger jusqu'à 11 ans et demi *(cf. graphique 4)*. A 12 mois, 3 cicatrisations sur 46 sont observées et la probabilité d'avoir des cicatrisations incomplètes ou des échecs à cette période est encore de 0.963.

A 2 ans, 22 dents traitées présentent une régression totale ou sub-totale de leur lésion apicale et la probabilité de non-cicatrisation est alors inférieure ou égale à **0.688**.

La **médiane de survie est à 42 mois** (3 ans et demi), ce qui signifie que la moitié de l'échantillon a totalement cicatrisé à cette période *(cf. tableau 7).* **A 4 ans**, la probabilité de non-cicatrisation n'est plus que de **0.363**, ce qui signifie que 63.7% des lésions apicales ont disparu. **A 81 mois** (presque 7 ans), **24%** des lésions n'ont pas encore totalement cicatrisé. A 9ans, la probabilité d'échec ou de cicatrisation incomplète n'est plus que 0.08.

Groupe AP+ N = 105
Nombre de succès = *46* Médiane de cicatrisation = ***43 mois*** Temps moyen de cicatrisation = *53 mois* Quantiles : *75% à 21 mois* *48% à 43 mois* *24% à 81 mois*

Tableau 7: *Médiane, moyenne et quantiles de survie de la cicatrisation périapicale.*

2.2.2. Détermination des facteurs pronostiques :

Nous avons utilisé la même procédure que celle utilisée dans la précédente étude.

L'analyse univariée grâce à des tests du Log Rank permet d'évaluer de l'implication de chaque paramètre, ***indépendamment les uns des autres***, sur l'apparition de pathologie périapicale pour le groupe AP-, l'échec thérapeutique et la cicatrisation apicale pour le groupe AP+.

A partir de ces tests univariés, nous obtenons une sélection de variables avec un seuil de signification à $p < 0.20$; ces variables sont intégrées dans des modèles multivariés de Cox où ***elles sont évaluées ensemble***. Par méthode pas à pas ascendante et descendante, nous obtenons un modèle de Cox final avec un ensemble de variables impliquées dans le succès ou l'échec thérapeutique des 2 populations AP- et AP+ au seuil de signification $p<0.05$. [2]

2.2.2.1. Facteurs pronostiques de l'échec thérapeutique :

2.2.2.1.1. Population sans pathologie périapicale initiale (AP-) :

Pour l'analyse du lien entre les différents facteurs pronostiques et l'évolution défavorable du traitement ou l'apparition de pathologie périapicale, l'événement étudié est **l'échec**. Les succès et les cas incertains seront considérés comme absence d'évènement.

2.2.2.1.1.1. Analyse univariée : *Tableau 8: Analyse univariée du lien entre l'échec et les facteurs étudiés dans le groupe sans pathologie périapicale initiale (AP-)*

Facteurs	Risque relatif (RR)	Test statistique: Log Rank		
		Valeur	ddl	Probabilité
Localisation maxillaire ou mandibulaire	*0.904*	*0.359*	*1*	*0.549*
Localisation antérieure ou postérieure	*0.765*	*0.048*	*1*	*0.826*
Complexité anatomique	***1.826***	*4.450*	*1*	***0.035***
Nombre de canaux		*10.457*	*3*	***0.015***
Monoradiculées / pluriradiculées	*1.771*	*3.255*	*1*	*0.071*
Courbure canalaire	*0.347*	*1.790*	*1*	*0.181*
Calcification canalaire	***2.328***	*6.604*	*1*	***0.010***
Canal supplémentaire	***5.23***	*5.090*	*1*	***0.024***
Pathologie aigue	***1.958***	*1.111*	*1*	*0.292*
Indication prothétique	*0.536*	*1.898*	*1*	*0.168*
Pathologie traumatique	*3.364*	*0.533*	*1*	*0.465*
Retraitement endodontique	*0.413*	*0.994*	*1*	*0.319*
Niveaux de compétence des intervenants		*2.514*	*2*	*0.285*
Correspondance entre niveau d'obturation et longueur de travail	***4.154***	*0.100*	*1*	*0.752*
Qualité d'obturation	*1*	*0.785*	*1*	*0.376*
Sur obturation canalaire	*1.298*	*0.004*	*1*	*0.952*
Sous obturation canalaire	*0.903*	*0.956*	*2*	*0.620*
Qualité / étanchéité de la restauration coronaire	***25.412***	*19.575*	*1*	***<0.001***
Type de restauration coronaire (provisoire ou définitive)	***0.093***	*51.724*	*1*	***<0.001***
Technique de préparation endocanalaire	*0.780*	*0.052*	*1*	*0.819*
Technique d'obturation endocanalaire	*0.667*	*0.270*	*1*	*0.603*
Obturation immédiate	*1.429*	*0.376*	*1*	*0.540*
Iatrogénie	***7***	*11.656*	*1*	***0.001***
Présence d'une perforation	***19.138***	*4.910*	*1*	***0.027***
Présence d'un faux canal	***0.810***	*7.532*	*1*	***0.006***
Présence de débris instrumental	***3.317***	*21.315*	*1*	***<0.001***
Médication d'interséance		*1.753*	*3*	*0.625*

$P \leq 0.05$: lien significatif

Pour le groupe AP-, l'analyse univariée *(cf. tableau 8)* fait apparaitre un lien significatif entre l'échec thérapeutique et plusieurs facteurs : complexité de l'anatomie endocanalaire

(p=0.035), le nombre de canaux *(p=0.015),* la présence de canaux supplémentaires *(p=0.024),* la présence de calcification *(p=0.010),* la qualité et le type de restauration coronaire, l'iatrogénie *(p=0.001),* la présence d'une perforation *(p=0.027),* la présence d'un faux canal *(p=0.006),*la présence d'un fragment instrumental *(p<0.001).*

2.2.2.1.1.2. Modèle de Cox final :

Lors de la réalisation du modèle de Cox final pour la mise en évidence des facteurs prédictifs de l'échec dans le groupe AP- apparait une colinéarité des facteurs *localisation maxillaire mandibulaire* et *du niveau de compétence*. En effet, le taux d'échec augmente sur les dents maxillaires et est inversement proportionnel au niveau de compétence du soignant. Nous avons étudié différents modèles possibles et nous avons proposé un modèle avec stratification sur le *niveau de compétence.*

Facteurs prédictifs	p-value
Monocanalaire / Pluricanalaire	0.100
Canal supplémentaire	**<0.001**
Sous obturation	**0.007**
Etanchéité de la restauration coronaire	0.062
Type de restauration coronaire	**<0.001**
Technique de préparation canalaire	**0.002**

***Tableau 9** : Modèle de Cox final : facteurs liés à l'échec thérapeutique dans le traitement endodontique des dents sans pathologie périapicale initiale. (AP-)*

Les facteurs prédictifs de l'échec des traitements sur dents sans pathologie périapicale initiale sont donc la présence d'un **canal supplémentaire** *(p<0.001)*, la présence d'une **restauration coronaire provisoire** *(p<0.001),* la **préparation manuelle** par rapport à la préparation en

rotation continue *(p=0.002)* et la **sous obturation** *(p=0.007) (cf. tableau 9).*

2.2.2.1.2. Population avec pathologie périapicale initiale (AP+) :

2.2.2.1.2.1. Analyse de survie univariée :

***Tableau 11**: Analyse univariée du lien entre **l'échec thérapeutique** et les facteurs étudiés dans le groupe avec pathologie périapicale initiale (AP+).*

Test statistique: Log Rank	**RR**	Valeur	ddl	Probabilité
Localisation maxillaire ou mandibulaire	*1.418*	*0.787*	*1*	*0.375*
Localisation antérieure ou postérieure	*0.685*	*0.447*	*1*	*0.504*
Complexité anatomique	*1.096*	*0.505*	*1*	*0.477*
Nombre de canaux		*0.351*	*3*	*0.314*
Monoradiculées / pluriradiculées	*1.467*	*2.340*	*1*	*0.126*
Courbure canalaire	*0.774*	*0.414*	*1*	*0.520*
Calcification canalaire	*0.674*	*0.227*	*1*	*0.634*
Canal supplémentaire	*1.571*	*2.708*	*1*	*0.1*
PAI initial		*8.192*	*2*	***0.017***
Pathologie aigue	*0.844*	*0.001*	*1*	*0.988*
Pathologie chronique	*2.089*	*2.849*	*1*	*0.091*
Indication prothétique	*0.224*	*5.156*	*1*	*0.023*
Pathologie traumatique		*0.427*	*1*	*0.514*
Lésion endo-parodontale	*1.584*	*0.222*	*1*	*0.637*
Image périapicale	***3.069***	*8.732*	*1*	***0.003***
Volume de l'image périapicale		*15.647*	*7*	***0.029***
Retraitement endodontique	*0.624*	*1.687*	*1*	*0.194*
Niveaux de compétence des intervenants		*1.632*	*2*	*0.442*
Correspondance entre niveau d'obturation et longueur de travail	***6.642***	*16.911*	*1*	***<0.001***
Qualité d'obturation	*1.034*	*0.769*	*1*	*0.380*
Sur obturation canalaire	*1.232*	*1.407*	*1*	*0.236*
Sous obturation canalaire	*0.942*	*0.184*	*2*	*0.668*
Qualité / étanchéité de la restauration coronaire	***20.8***	*7.689*	*1*	***0.006***
Type de restauration coronaire (provisoire ou définitive)	***29.189***	*21.245*	*1*	***<0.001***
Technique de préparation endocanalaire	*6.642*	*0.893*	*1*	*0.345*
Obturation immédiate	*1.147*	*0.069*	*1*	*0.793*
Iatrogénie	*2.691*	*2.428*	*1*	*0.119*
Présence d'un faux canal	*1.041*	*0.839*	*1*	*0.360*
Présence de débris instrumental		*1.540*	*1*	*0.215*
Butée		*0.131*	*1*	*0.718*
Médication d'interséance		*1.7377*	*2*	*0.420*

Cause d'échecs		*13.208*	*6*	***0.040***

$p \leq 0.05$: lien significatif

Pour le groupe AP+, l'analyse univariée fait apparaitre un lien significatif entre l'échec thérapeutique et plusieurs facteurs : le Periapical Index (PAI) initial élevé *($p=0.017$)*, la présence d'une image radioclaire de lyse osseuse *($p=0.003$)*, le volume de l'image radioclaire périapicale *($p=0.029$)*, l'absence de correspondance entre niveau de préparation et d'obturation *($p<0.001$)*, la qualité *($p=0.006$)* et le type de restauration coronaire *($p<0.001$) (cf. tableau 11).*

2.2.2.1.2.2. Modèle de Cox final :

Les facteurs prédictifs de l'échec des traitements sur dents avec pathologie périapicale initiale sont donc la présence d'une **restauration coronaire provisoire** *($p<0.001$)*, **le volume de l'image radioclaire périapicale** *($p=0.025$)*, **l'absence de correspondance** entre niveau de préparation et d'obturation *($p=0.006$) (cf. tableau 10).*

Facteurs impliqués dans l'échec thérapeutique	p-value
Volume de l'image apicale	**0.025**
Correspondance entre longueur de travail et niveau d'obturation	**0.006**
Type de restauration coronaire (provisoire / définitive)	**<0.001**
Canal supplémentaire	0.088

***Tableau 10**: Modèle de Cox pour le groupe avec pathologie périapicale initiale (AP+).*

2.2.2.2. Facteurs pronostiques de la cicatrisation périapicale :

2.2.2.2.1. Analyse de survie univariée :

***Tableau 13** : Analyse univariée du lien entre la **cicatrisation apicale** et les facteurs étudiés dans le groupe avec pathologie périapicale initiale (AP+).*

Test statistique: Log Rank	RR	Valeur	ddl	Probabilité
Localisation maxillaire ou mandibulaire	*0.528*	*0.389*	*1*	*0.533*
Localisation antérieure ou postérieure	***1.327***	*5.597*	*1*	***0.018***
Complexité anatomique	*1.153*	*3.540*	*1*	*0.060*
Nombre de canaux		*5.641*	*3*	*0.130*
Monoradiculées / pluriradiculées	*0.741*	*2.085*	*1*	*0.149*
Courbure canalaire	***2.864***	*10.641*	*1*	***0.001***
Calcification canalaire	*1.314*	*2.003*	*1*	*0.157*
Canal supplémentaire	*1.4*	*0.569*	*1*	*0.451*
PAI initial		*5.081*	*2*	*0.079*
Pathologie aigue	*0.730*	*1.403*	*1*	*0.236*
Indication prothétique	*2.035*	*1.001*	*1*	*0.317*
Pathologie traumatique		*1.524*	*1*	*0.217*
Lésion endo-parodontale	*1.585*	*2.732*	*1*	*0.098*
Volume de l'image périapicale		*9.452*	*4*	***0.051***
Retraitement endodontique	*1.210*	*0.717*	*1*	*0.397*
Niveaux de compétence des intervenants		*0.591*	*2*	*0.744*
Correspondance entre niveau d'obturation et longueur de travail	*0.205*	*0.008*	*1*	*0.930*
Qualité d'obturation	*0.726*	*1.178*	*1*	*0.278*
Sur obturation canalaire	*0.758*	*0.049*	*1*	*0.825*
Sous obturation canalaire	*0.911*	*2.260*	*2*	*0.133*
Qualité / étanchéité de la restauration coronaire	***0.125***	*3.886*	*1*	***0.049***
Type de restauration coronaire (provisoire ou définitive)	***14.667***	*6.911*	*1*	***0.009***
Technique de préparation endocanalaire	***1.287***	*25.165*	*1*	***<0.001***
Obturation immédiate	*0.632*	*1.180*	*1*	*0.277*
Iatrogénie	*0.459*	*0.092*	*1*	*0.762*
Présence d'un faux canal	*0.333*	*0.026*	*1*	*0.872*
Présence de débris instrumental	*0.452*	*0.660*	*1*	*0.417*
Médication d'interséance		*4.007*	*2*	*0.135*

$p \leq 0.05$: lien significatif

La cicatrisation périapicale semble favorisée par: la technique de préparation canalaire utilisée *(p<0.001)*, la qualité *(p=0.049)* et le type de restauration coronaire *(p=0.009)*, la présence de courbure canalaire *(p=0.001)*, la localisation antérieure de la dent *(p =0.018)* et volume de l'image périapicale *(au seuil de signification, p=0.051) (cf. tableau 13).*

2.2.2.2.2. Modèle de Cox final :

Le modèle de Cox *(cf. tableau 12)* met en évidence 4 facteurs prédictifs de la cicatrisation apicale: la mise en place d'une **restauration définitive adaptée** *(p=0.017)*, l'utilisation de technique de préparation par **rotation continue** *(p<0.001)*, **l'absence de courbure significative** *(p = 0.042)*, ainsi qu'**un niveau de compétence élevé** *(p = 0.025).*

Facteurs impliqués dans la cicatrisation apicale	p-value
Type de restauration coronaire	**0.017**
Technique de préparation	**<0.001**
Courbure canalaire significative	**0.042**
Indication Prothétique	0.071
Niveau de compétence	**0.025**
Localisation antérieure-postérieure	0.066

Tableau 12*: Modèle de Cox pour le groupe avec pathologie périapicale initiale (AP+).*

Avec stratification sur le niveau de compétence *(cf. tableau 13)*, seuls restent comme facteurs prédictifs de la cicatrication périapicale **: la restauration ou reconstitution coronaire définitive** *(p=0.011)* la technique de préparation endocanalaire par **rotation continue** *(p<0.001)* et l'indication de traitement pour **raison prothétique** *(p = 0.022).*

Facteurs impliqués dans la cicatrisation apicale	p-value
Type de restauration coronaire	**0.011**
Technique de préparation	**<0.001**
Indication Prothétique	0.022

Tableau 13*: Modèle de Cox fina,l stratifié sur le niveau de compétence, pour le groupe avec pathologie périapicale initiale (AP+)*

3. Discussion :

3.1. Analyse des biais et répercussion sur les résultats :

La population observée a été recrutée par tirage au sort à partir des patients inscrits en polyclinique. Le tirage au sort nous a permis de faire un échantillonnage représentatif de la patientèle suivi au Centre de Soins Dentaires de Nantes pour traitement pluridisciplinaire. Le tirage au sort s'est fait sur une population bénéficiant ou devant bénéficier d'un traitement global pour réhabilitation de la cavité buccale. Ces patients sont engagés dans un processus de soins long et nous assure la possibilité de pouvoir suivre au long cours le résultat de nos thérapeutiques endodontiques sans perdus de vue, ou avec un taux de réponse faible, ce qui est l'un des facteurs limitatifs dans l'évaluation des thérapeutiques endodontiques [132].

Par ailleurs, l'aspect prospectif de notre seconde cohorte nous a permis de connaitre précisément l'état pathologique initial et les indications qui ont motivés les traitements endodontiques, les conditions de réalisation de ces traitements, de pouvoir identifier les traitements non achevés pour iatrogénie et de connaitre précisément les raisons et le moment de survenue de l'échec (extraction, retraitement orthograde et chirurgical).

Si le choix d'une étude longitudinale avec tirage au sort des patients nous permet d'éviter des biais de recrutement [132], il présente néanmoins l'inconvénient d'un recrutement et d'un suivi sur plusieurs années. Les derniers recrutements, afin d'obtenir plus de 250 traitements et une puissance d'analyse suffisante, se sont réalisés en 2010 ; l'arrêt de l'étude en juillet 2011.

3.2. Réponse aux questions posées :

Le choix de l'analyse statistique est primordial dans ce contexte; une analyse de survie est plus indiquée qu'une régression logistique pour notre étude de cohorte, puisque le temps de suivi d'un patient à l'autre est très variable. En effet, nous n'avons pas voulu imposer aux patients une ou plusieurs consultations de suivi de nos thérapeutiques endodontiques, mais profiter de leurs rendez-vous dans le cadre de leur prise en charge pluridisciplinaire pour réaliser nos réévaluations. L'analyse de survie par modèle de Cox autorise ces différences de temps de suivi entre les sujets. Par ailleurs, l'avantage des analyses de survie est de pouvoir utiliser les informations de la date de point (dernière date d'évaluation ou de fin d'étude) que l'on soit en présence ou non de l'évènement attendu. Ceci est particulièrement intéressant dans le cadre de l'étude de la cicatrisation périapicale dans le temps. Ainsi, même si le processus cicatriciel est en cours mais non achevé à un instant précis, il sera noté comme absence de l'évènement attendu et pris en compte dans l'analyse. Lors de la cicatrisation complète, l'évènement sera analysé en fonction du paramètre temps de suivi et permettra le

calcul d'une probabilité de survie. L'analyse de survie est donc particulièrement indiquée pour suivre la cicatrisation périapicale dans le temps [95].

Bien que certains auteurs utilisent [66] [133] et préconisent le score PAI [74] pour l'évaluation du pronostic thérapeutique en endodontie, l'utilisation d'un critère exclusivement radiographique peut entrainer la surestimation des résultats thérapeutiques [132]. L'appréciation du succès d'un traitement endodontique doit se faire sur l'absence de signes cliniques et radiologiques pathologiques [67-69, 76] associée à la récupération d'une dent fonctionnelle [22, 107].

Comme pour la première étude de cohorte et conformément aux précédents résultats obtenus, nous avons délibérément scindé la population cible en 2 sous-groupes pour éviter d'analyser une population hétérogène tant au niveau de la pathologie initiale que de la réponse au traitement. La période de suivie moyenne est respectivement de **2 ans et 10 mois ± 2 ans et 8 mois** pour les dents sans pathologie périapicale initiale (AP-) et de **2 ans et 3 mois ± 2 ans et 1 mois** pour les dents avec lésion périapicale initiale (AP+) (contre 2ans 4 mois ± 9 mois pour (AP-) et 2ans 5 mois ± 9 mois pour (AP+) dans la première étude).

Le délai de réévaluation des traitements endodontiques s'échelonne de 0 à 171 mois (plus de 14 ans) avec un nombre de suivis allant de 0 (iatrogénie avec échec immédiat) à 6 consultations de réévaluation.

Au terme de l'étude, le succès thérapeutique est observé pour **71.9**% des dents traitées sans pathologie périapicale initiale contre **41.8%** des dents avec pathologie périapicale. Si les résultats obtenus confirment ceux de la littérature qui rapporte un meilleur taux de succès sur les dents sans pathologie périapicale [19, 52, 56, 58, 59, 62, 64, 66-68, 70, 71, 106], ils demeurent beaucoup moins élevés que ceux de la première étude **(89.2%** et **67.7%)**. Ceci pourrait s'expliquer par le fait que le recrutement de la population s'est fait différemment dans les 2 études. Le recrutement sur la base du volontariat aurait tendance à inclure des sujets

significativement différents des perdus de vus et des non-répondants, et à surestimer le taux de succès des thérapeutiques endodontiques [74].

Par randomisation, ce biais de recrutement est écarté.

Néanmoins, un autre paramètre peut expliquer cette baisse du taux de réussite des traitements endodontiques dans la seconde étude : c'est la prise en compte de tous les traitements endodontiques réalisés chez nos patients, non seulement ceux achevés mais aussi ceux qui se sont soldés par la perte de la dent avant obturation. C'est le cas de traitements en cours avec plusieurs épisodes infectieux successifs et ceux avec iatrogénie. L'iatrogénie ayant entrainé l'extraction de la dent est un facteur négligé ou sous-estimé dans les études des facteurs prédictifs de l'échec en endodontie, d'autant plus dans les études rétrospectives [63, 134]. Dans notre cohorte prospective, l'iatrogénie concerne 10% des traitements réalisés au Centre de Soins Dentaires avec 8% de thérapeutiques endodontiques iatrogènes dans le groupe AP- et 14% dans le groupe AP+. L'iatrogénie est la cause majeure d'échecs précoces dans les 2 groupes. En effet, le Risque Relatif d'échec lié à l'iatrogénie est de 7 dans le groupe AP- *(Log Rank, p<0.001),* et de 2.691 dans le groupe AP+ *(Log Rank, p=0.119).* Dans le groupe des dents avec pathologie périapicale initiale (AP+), l'iatrogénie n'apparait pas comme facteur prédictif significatif car l'analyse de survie a été réalisée après délétion de 7 sujets présentant un temps de survie = 0 et dont l'échec était lié directement à un traitement iatrogène.

Le facteur impliqué dans l'échec des traitements endodontiques des 2 groupes est la restauration ou reconstitution provisoire *(p<0.001).* De nombreux auteurs ont rapporté que l'absence d'une **restauration coronaire pérenne et adaptée** est un facteur prédictif important de l'échec thérapeutique en endodontie [83, 84, 89, 107-111, 135]. Le modèle de Cox réalisé pour le succès thérapeutique des dents (AP+) conclue en ce sens puisque la cicatrisation périapicale semble favorisée par la mise en place d'une restauration coronaire ou d'une reconstitution corono-radiculaire étanche *(p=0.049)* et définitive *(p=0.009).*

Quelque soit la pathologie initiale de la dent traitée, l'absence de restauration ou de reconstitution coronaire définitive et étanche fait chuter considérablement le temps et la probabilité de survie : de 120 mois (médiane de survie à 108) à 34 mois seulement (médiane de survie à 21) pour le groupe (AP-) et de 91 mois (médiane de survie à 108) à 32 mois (médiane de survie à 21).

Lorsque nous regardons les modèles de Cox finaux, le type de restauration coronaire est associée à d'autres facteurs prédictifs de l'échec tels que : une sous-obturation et un canal oublié pour le groupe (AP-) et l'absence de correspondance entre la longueur de travail et la longueur d'obturation. Les résultats de notre cohorte sont concordants avec ceux de la littérature dans ce domaine [63, 131, 134-137] concluant que le risque d'échec s'exprime réellement avec **l'association d'une obturation endodontique insuffisante (au niveau de la condensation et/ou de la longueur d'obturation) et l'absence d'étanchéité coronaire.** Nous avons pu constater que les risques d'échec étaient minimisés avec une mise en fonction précoce par restauration coronaire ou reconstitution corono-radiculaire définitive.

Néanmoins dans notre cohorte, de nombreuses extractions liées à l'absence de restauration coronaire ou de reconstitution coronoradiculaire définitive et adaptée sont souvent secondaires à une perte de substance par reprise de carie, plus qu'à l'apparition de pathologie périapicale. Le manque d'étanchéité coronaire apparait dans ce cas précis comme un facteur de confusion [111], la cause réelle d'extraction étant la perte de substance corono-radiculaire et non la contamination bactérienne de l'endodonte et du périapex. Dans notre étude, il n'y a pas eu de développement objectif d'une pathologie périapicale après perte de l'étanchéité coronaire.

Nous avons intégré le volume de la lésion périapicale dans l'étude des facteurs prédictifs du groupe (AP+). Notre analyse montre l'impact du volume de la lésion initiale sur le risque d'échec conformément aux conclusions de certains travaux [58]. Néanmoins, même si les

clichés rétroalvéolaires ont toujours été pris selon une incidence orthocentrée, nous savons aujourd'hui que l'évaluation des dimensions de l'image radiographique par cette technique radiographique a ses limites [131, 132].

Nous avons voulu évaluer l'influence du **nombre de séances de traitement** et l'utilisation d'hydroxyde de calcium comme **médication intra-canalaire** sur la survie des traitements endodontiques et la cicatrisation périapicale. Auparavant, l'hydroxyde de calcium était préconisé en inter-séance pour prévenir ou réduire le développement bactérien dans le canal, dans le but de consolider l'action de la préparation chémo-mécanique et de l'irrigation intra-canalaire dans la décontamination de l'endodonte [133, 138-140]. Plusieurs auteurs ont prouvé que l'hydroxyde de calcium n'était pas efficace pour maintenir l'asepsie intra-canalaire [88, 133, 141]. Le bénéfice de l'hydroxyde de calcium sur la cicatrisation periapicale n'a pas non plus été mis en évidence [81, 82, 88, 142-144]. Nos résultats coïncident avec ceux déjà publiés, puisque le nombre de séances de traitement, ainsi que la médication intra-canalaire ne semblent ni influer sur la survie des traitements endodontiques, ni sur la cicatrisation périapicale.

D'autres facteurs ont été évalués dans cette étude notamment le **niveau de compétence** du soignant [59, 114], les **techniques de préparation**, facteurs prédictifs évoqués dans d'autres études [46, 57, 65, 67, 68, 70, 71]. Notre première étude n'avait pu conclure à l'amélioration du pronostic avec l'instrumentation Nickel Titane par biais d'indication ; en effet, cette technique était indiquée de façon marginale pour des étudiants expérimentés en endodontie, lorsque la complexité canalaire empêchait l'utilisation de techniques de préparation manuelles.

Cette cohorte prospective s'est réalisée avec l'utilisation plus répandue de l'instrumentation Nickel Titane en rotation continue pour la préparation endocanalaire.

La proportion de traitements réalisés avec ce genre de technique est d'environ 50%, et les résultats observés montrent une probabilité de survie nettement améliorée, quelque soit la pathologie initiale. Néanmoins; l'accumulation de facteurs défavorables (difficulté d'accès, lésion apicale, complexité de l'anatomie de l'endodonte..) reste encore associées à l'augmentation du niveau de compétence et de technicité. Pour cette raison, nos modèles de Cox finaux sont réalisés avec stratification sur le niveau de compétence. La technique de préparation apparait dans les 2 groupes comme un facteur prédictif important, conformément à certaines études [67-69]. L'utilisation d'instruments en Nickel Titane permet de réaliser une ampliation en respectant l'anatomie canalaire, mais également de réduire la réduction du nombre de bactéries intra-canalaires en optimisant l'irrigation et la désinfection du tiers apical [139, 145].

Le niveau de compétence a également un impact sur les résultats à long terme des traitements endodontiques [19], puisque les étudiants inexpérimentés peuvent plus fréquemment être à l'origine de traitements iatrogènes. Les renseignements obtenus dans cette étude prospective le confirment. Même si les résultats de la cohorte prospective semblent modestes, ils sont cependant comparables à ceux publiés précédemment à partir de traitements endodontiques réalisés par des étudiants [61], avec une survie de 56% à 6,2ans. Notre analyse évalue la survie au même délai à environ 45% pour le groupe AP+, et à plus de 66% pour le groupe AP-.

3.3. De l'intérêt des résultats par rapport à ceux déjà publiés dans ce domaine:

L'utilisation de modèles d'analyse de survie permet d'obtenir des informations que ne peuvent fournir d'autres analyses multivariées telles que la régression logistique ; en effet nous pouvons suivre la probabilité de survie dans le temps, calculer la moyenne de survie et obtenir la dispersion de l'échantillon en fonction du temps grâce aux quantiles. Nos résultats

montrent que la survenue de l'échec thérapeutique semble plus précoce dans la population avec pathologie périapicale (groupe AP+) **puisque la médiane de survie est de 53 mois contre 93 mois pour le groupe (AP-)**, *soit un gain de survie de plus de 3 ans.* Ceci signifie que la moitié des échecs est observé à 53 mois dans le groupe (AP+) contre 93 mois pour le groupe (AP-). A 9 ans, la probabilité de survie n'est plus que de 24% dans la population avec pathologie périapicale initiale (AP+) contre 37 % dans le groupe sans pathologie périapicale initiale (AP). Là encore, nos résultats confirment ceux de la littérature, concluant à l'impact de la pathologie initiale sur le pronostique des traitements endodontiques [19, 52, 56, 58, 59, 62, 64, 66-68, 70, 71, 106].

Comme nous l'avons expliqué précédemment, le choix de réaliser une analyse de survie sur les 2 groupes pris séparément **répond à une réalité clinique** qui est d'évaluer le pronostique des dents traitées sans pathologie périapicale initiale à partir l'apparition de symptômes et d'image radioclaire, et d'évaluer celui de dents traitées avec pathologie périapicale initiale à partir de la rémission ou de l'aggravation de symptômes et de l'image radioclaire préexistants. L'analyse de survie permet ce genre d'analyse en prenant en compte la *survenue de l'évènement attendu* dans le temps, tout autre évènement étant noté comme *absence de l'évènement attendu* et censuré à droite. Ce type d'analyse est particulièrement intéressant pour suivre des processus de guérison sur une longue période, ce qui est adapté à la cicatrisation périapicale. La cicatrisation périapicale a été déjà étudiée en prenant en compte les états intermédiaires de cicatrisation. Ainsi Orstavik en 1996 [53] concluait que 89% des cicatrisations périapicales, même incomplète, était observée à 1 an. Or, l'utilisation de technique telle que le Cone Beam met en évidence les limites de l'évaluation de la cicatrisation par rétroalvéolaire [131, 132], d'autant plus si elle se base sur un état intermédiaire : *« une cicatrisation initiée mais incomplète »* [53]. Etant donné que notre étude

a commencé au moment où ce genre de technique n'était pas disponible et qu'actuellement, en France, l'utilisation du Cone Beam de manière courante en endodontie est encore inenvisageable, il apparait évident que le processus cicatriciel apprécié à partir de radiographies rétroalveolaires doit se faire sur l'obtention d'une cicatrisation totale du périapex, c'est-à-dire le retour à une image de la zone périapicale normale. Toute observation, quelque soit le volume de l'image initiale, mettant en évidence une zone radioclaire résiduelle ou une condensation osseuse et ceci, même en présence de remaniement osseux laissant présager une cicatrisation en cours, sera comptabilisé comme « *absence de cicatrisation complète* » dans l'analyse de survie. Cette évaluation nous permet 1°) d'éviter ou de limiter toute surestimation du succès de la thérapeutique endodontique sur dents avec pathologie périapicale initiale, 2°) de prédire l'évolution dans le temps de la cicatrisation périapicale.

Notre analyse a mis en évidence un temps de cicatrisation variant de 10 à 138 mois (soit onze ans et demi), période durant laquelle tous les succès avec disparition totale de l'image radioclaire sont recensés.

Ces résultats ne sont pas concordants avec ceux d'Orstavik en 1996, pour qui la majorité des lésions périapicales guérissaient dans la première année (89%). Notre étude conclue à un temps de cicatrisation moyen à un peu plus de 4 ans (53 mois).

La probabilité de cicatrisation avant deux ans (21 mois) est de 0.25, ce qui signifie que seulement un quart des cicatrisations périapicales complètes surviennent la première année ; la moitié des dents traitées avec cicatrisation complète est observée à 43 mois, 76% à 81 mois.

Comme pour l'étude précédente, les résultats de cette cohorte prospective suggèrent que les délais de réévaluation préconisés [99, 118] pourraient être trop courts pour pouvoir se prononcer sur la réussite à long terme des thérapeutiques endocanalaires, notamment en ce qui concerne la cicatrisation périapicale. Certains auteurs [76, 88, 95] conseillent un temps de

suivi de 4 à 5 ans minimum pour pouvoir s'assurer du bon déroulement du processus cicatriciel. Peu d'études ont suivi les sujets jusqu'à cicatrisation périapicale complète [76, 84, 107].

4. Conclusion :

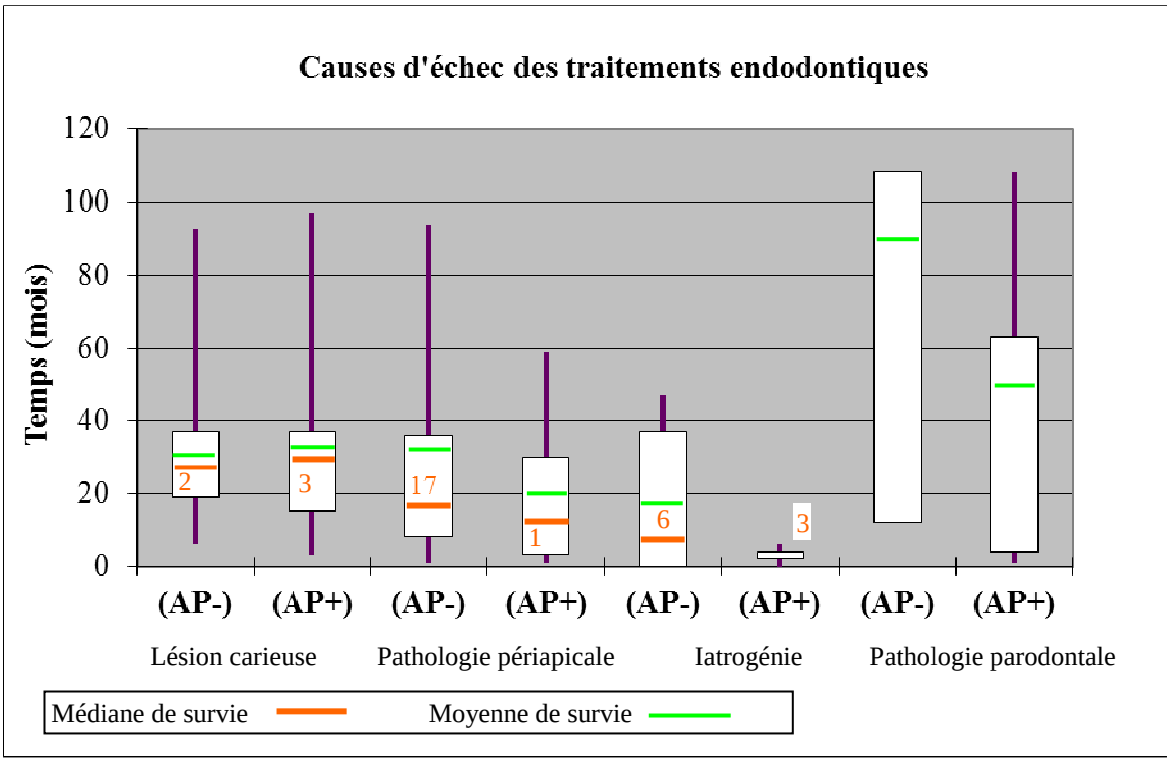
Cette deuxième cohorte montre que l'échec des thérapeutiques est favorisé par **l'absence de restauration coronaire ou reconstitution corono-radiculaire précoce étanche et définitive associée à un défaut d'obturation endodontique**, quelque soit la pathologie initiale. La préparation par **rotation continue** semble également améliorer le pronostic.

Au niveau du temps de réévaluation, nos résultats montrent que **le suivi à un an selon les recommandations** [99, 118] **peut s'avérer inefficace en terme de prédiction du pronostic à long terme des thérapeutiques endodontiques** car seulement 6% des échecs sont observés à cette période dans le groupe de dents traitées sans pathologie périapicale initiale et 17% dans le groupe de dents traitées avec pathologie périapicale initiale. A 12 mois, seules 5.6% des cicatrisations périapicales complètes sont constatées.

Pour les cas incertains, une seconde évaluation est préconisée à 4 ans. A cette période, notre étude montre que 30% des échecs ont été observés pour le groupe (AP-), 45% pour le groupe (AP+) ainsi que 62% des cicatrisations périapicales.

Les **échecs tardifs** existent et sont essentiellement liés aux caries secondaires par perte d'étanchéité coronaire et surviennent pour la grande majorité à partir de 2 ans. Les autres causes d'échec tardif sont parodontales et endo-parodontales.

Les **échecs précoces** sont liés à l'iatrogénie objectivés dans les 6 premiers mois et à l'apparition ou à la progression d'une pathologie périapicale qui sont constatés dans les 4 années suivant le traitement. En effet pour les dents sans pathologie périapicale, 77% des apparitions d'image apicale seront observées avant 30 mois. Pour les dents avec pathologie périapicale initiale, plus de la moitié des échecs d'étiologie endodontique survient lors de la première année et 75% avant 36 mois.



Graphique 5 : Représentation en Box Plot de la répartition au cours du temps des échecs en fonction de leurs causes.

*Cette représentation donne les **valeurs de médiane de survie** (en rouge) et permet de visualiser les valeurs minimales et maximales de temps auxquelles apparaissent le premier et dernier échec (extrémités des traits verticaux inférieurs et supérieurs), ainsi que les 25 et 75 percentiles (extrémités des boîtes).*

Ce graphe nous montre que l'évaluation à 1 an permet uniquement de mettre en évidence la majorité des échecs liés à l'iatrogénie. Il montre également que le moment de l'évaluation est important et surtout qu'il est différent selon les causes d'échec incriminés.

Par ailleurs, la réévaluation clinique et radiographique de la thérapeutique endodontique selon les recommandations professionnelles n'est valable que dans l'hypothèse où leurs résultats n'évoluent plus au terme de la première année pour la grande majorité d'entre-deux, et de 4 ans pour les cas incertains. Or, l'utilisation des modèles de survie a contribué largement à prouver que le pronostic des traitements endodontiques est loin d'être figé au terme des 4 ans et continue d'évoluer bien des années après. De plus, la survie à long terme des traitements endodontiques est nettement plus faible que celle des dents non traitées [78, 146] et ne cesse de décroître au fil du temps [59, 134, 147].

Cette constatation nous amène à envisager d'autres alternatives thérapeutiques aux traitements endodontiques conventionnelles.

Partie III: Article

Prognosis factors influencing the long-term survival of endodontically treated teeth and the periapical healing: a prospective study

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Introduction

Relevant knowledge on the outcome of root canal treatment is necessary to clinical decisions, especially when retention of root canal treated teeth is opposed to extraction and replacement. Systematic reviews [41, 85] and meta-analyses [81, 83, 84, 86, 87, 107, 116] were recently proposed to identify the most important factors influencing endodontic treatment outcome. Only several clinical trials and well-controlled cohort studies are being considered as the current basis for evidence of the outcome and prognosis of initial root-canal treatment [38, 39]. While the complete elimination of microorganisms from the root canals is widely established as the key of successfull outcome of endodontic therapy [44, 64, 97, 106, 148, 149], several technical and clinical variables should directly or indirectly influence the prognosis of root canal treatments. Longitudinal studies have shown that infected pulp and preoperative apical periodontitis are the main predictive factors [51, 58, 64-69, 71, 106] and suggested that the filling quality would only significantly affect the prognosis of teeth with initial apical periodontitis [44, 46, 56, 70]. More recently, the debate concerns the influence of coronal restorations on long-term endodontic therapy outcome [136, 137] faced on conclusions that periapical health depends significantly more on coronal restoration than on filling quality [110].

Multivariate methods have been developed to analyse the simultaneous influence of several variables on one dependent variable. Although logistic regression has been used to assess the relative effect of each variables suspected as possible failure factors [34, 58, 60, 63, 66-71, 74, 90, 91, 119] survival analysis has been

more rarely proposed [52, 56, 59, 61, 62, 134, 147]. Survival methods are more appropriate to assess dynamic and time-dependant processes [95] like the periapical healing and the appearance of an apical periodontitis. Moreover, survival analysis as Kaplan Meier [150], which estimates the probability that the event *failure* will not occur during a period, allows different recall times [147]. Multivariate analysis of potential risk factors affecting the outcome can adequately be achieved by Cox model [95].

The principal aim of this study is to assess the outcome of conventional endodontic treatment performed in the Dental Care Center of Nantes Public Hospital, after a minimum follow-up period of one year, which is recommended in the scientific literature [53, 99, 117, 118]. Based on previous results showing a different outcome according to the initial disease (pulpal or periapical) [45-47, 56, 58-60, 64-69, 74, 106], we managed to separately assess the treatments of patients with an initial apical periodontitis and those of patients without initial periapical disease This prospective cohort, using a contemporary statistical method, (i) quantifies the survival times of root canal treatments in each pathological group, and (ii) highlights the most predictive factors of both survival of treated teeth and periapical healing. A multivariate survival analysis with a Cox model is proposed to evaluate the simultaneous influence of several technical, biological and technical variables on the treatment outcome: *e.g*. initial pathologic status, dental anatomy and situation, shaping or filling techniques, re-treatment, the skills of the practitioners, number of visits, filling extent and coronal restoration.

Materials and methods

Sample size

This study is a prospective cohort and not a clinical trial comparing the outcome of different treatment groups. The sample size cannot be calculated with the power analysis used by Trope et al [77]. For this study design, it was estimated with the Confidence Interval (5%) and the proportion of failure recorded in a previous assessment of the treatments performed in the Dental Care Center of Nantes Public Hospital (p=0.816; . 250 treatments were sufficient for powerful statistical results (>95%).

Studied population

The population of this prospective cohort was randomly selected from the patients treated for a pluri-disciplinary oral rehabilitation at the Nantes University Hospital. 107 patients were informed and equally invited to participate for one or several re-examinations of their root canal treatments performed by either under-graduate or post-graduate students under supervision, or qualified endodontists. Radiographic and clinical information

relating to the initial diagnosis of the treated teeth, the extent and the quality of the root canal filling, the shaping and filling techniques used as well as the grade of the student were prospectively recorded and controlled by the seniors in attendance. 256 root canal treatments were included.

Protocol of root canal therapy

Endodontic treatments were performed under controlled conditions and followed a standardized protocol. Root canals were cleaned and shaped using an aseptic technique and irrigated with 2.5% NaOCl. Root canal treatments were invariably achieved (i) either with stainless-steel hand file preparation and gutta-percha laterally condensation (ii) or with Rotary file preparation and either gutta-percha laterally condensation, either a Thermafil® or Herofil® filling for the most experienced students.

Follow-up examination

The assessment of endodontic outcome was performed at least one year after root canal filling and was repeated until the oral rehabilitation was totally achieved. To avoid additional appointments for the patients, we choose to assess the root canal treatments during their inter-disciplinary care. Moreover, the patients who had a complete oral rehabilitation are faithful to the Dental Center and the assessment of root canal treatments was possible during annual re-examinations.

The follow-up appointments consisted in a clinical and radiographic examination. Iinformation related to clinical pains, swelling, apical and gingival palpation and percussion. Status and the type of coronal restoration were also evaluated.

Radiographs were performed using the long-cone technique and standardized exposure to obtain optimal quality. Two independent observers separately analyzed the radiographs that had been calibrated prior to the study as described by Halse & Molven [120]**.** When disagreement occurred, a consensus was reached, according to Lambrianidis [121]**.** A higher percentage of agreement was found both in the interpretation of the periapical condition and the quality of the root canal seal when radiographs were simultaneously interpreted by both observers. The opinion of a third specialist was taken into account if the opinions of the two observers continued to differ.

Dependant variable: outcome of endodontic therapy

In accordance with the consensus on quality guidelines [117, 118] for endodontic treatment, we chose to assess the outcome of the treatment on both clinical and radiographic criteria. The periapical index (PAI) score was used to record the radiographic periapical status [105]. A PAI=0 was considered as an absence of a periapical disease. A score =1 was allowed for teeth with a pulpal vitality confirmed by clinical symptoms. Classification into the 2 different pathological groups was not strictly dependent on PAI score. One-year-results of root canal therapy were organized into 3 clinical situations: success, failure or uncertain cases [53, 99]. For analysis requirements and to predict both *survival of root canal treatments* and *periapical healing in time*, 2 events were observed during the follow-up period: (i) failure for all the patients, whatever the initial disease and (ii) success for patients with an initial periapical lesion (AP+).

- For patients with an initial periapical lesion, *success e.g. periapical healing* was defined as the absence of pain, swelling and other symptoms, sinus tract, loss of function, extraction or retreatment with the radiographic evidence of a normal periodontal ligament space or complete repair of periapical tissues. The other situations were considered as right-censored.
- For both groups (AP-) and (AP+), *failure* was defined as the appearance of a pathological periodontal ligament space or a periapical lesion, the persistence of clinical symptoms or the presence of continuing root resorption or hypercementosis, tooth extraction and re-treatment. The other situations were considered as right-censored.

The statistical unit was the tooth. In a multi-rooted tooth, the condition of the most severely affected root was recorded.

Independent variables: potential risk factors

The effect on the outcome of various parameters was evaluated, according to previous studies *[58, 61]*.

- *Tooth related factors*: localization on dental arch, number of root canals, complexity of root canal anatomy and the presence of severe curvatures or calcifications.
- *Practitioner's skill*: the undergraduate students *versus* the interns *versus* the qualified endodontists.
- *Initial pathology*: absence or presence of apical periodontitis, accurate or chronic symptoms, absence of any pulpal and periapical disease (root canal treatment for prosthetic reason or accidental pulpal exposure).

- *Treatment related factors*: initial root canal treatment *versus* re-treatment, number of sessions (immediate filling *versus* multiple-visits treatment), inter-appointment medication and presence of iatrogenic and procedural errors.
- *Technical factors*: shaping techniques (stainless-steel hand files preparation *versus* Ni-Ti rotary preparation) and filling techniques
- *Coronal status*: quality (absent or defective *versus* adequate) and type of coronary restoration (provisional *versus* definitive).
- *Filling related factors*: Extent of the root canal filling (flushed to 1mm to the apex, over-filling, under-filling), correspondence between working length and filling length, quality of filling condensation (hermetically sealed *versus* presence of voids).

Statistics

The analysis was performed by the SYSTAT 10.2 software version.

- A descriptive statistic analysis was firstly carried out for the total population and for each group: the one without initial periapical pathosis (AP-) and the one with apical periodontitis before root canal treatment (AP+).

  A comparison between these 2 groups was then conducted in order to detect differences in the repartition of prognosis factors (Chi square test).
- A monovariate survival analysis (Log-rank tests) was firstly performed to evaluate the association between the observed event and each factor. For the monovariate analyses, the alpha risk was set at 5% and 10% for the selection of variables in the Cox model.
- Then, a multivariate analysis was carried out by Cox Proportional Hazards Estimation to select the predictive factors of (i) endodontic failure in the total population and (ii) periapical healing in (AP+) group.

Results were expressed as the probability of predictive factors effect (i) in failure of root canal treatments for each group, and (ii) in periapical healing for the (AP+) group.

Survival curves showed the survival probability of endodontic therapy in each group, as well as the probability of failed or incomplete healing process over the time.

Results

Descriptive analysis

Out of the 107 treated patients, none was lost to follow-up. The mean of patient's age was 55 years old (± 16.23) and 52.34% were males. Our sample consists in 256 root canal treatments. The average number of treatments per patient was 2.39.

Out of 256 root canal treatments, 146 (57%) were teeth without periapical disease previous to treatment (AP- group) and 110 (43%) teeth with an apical periodontitis. (AP+ group). The mean follow-up period for the (AP-) group was about **34.2 ± 31.7 months** which represents a 1-to 5.5-year outcome. The mean follow-up period for the (AP-) group was about **27 ± 26.56 months** which represents a 1-to 4.5-year outcome. The early events recorded during the first year were related to tooth loss. The follow-up period is spread out from 0 to 171 months with 0 to 6 re-examination appointments *(table 1a).*

The descriptive analysis *(table 1b)* shows that, at the end of the study, failure has occurred for 23 % of treated teeth without initial periapical radiolucency (AP-) and for 39% of teeth with apical periodontitis (AP+). The success rate was lower than those announced in previous longitudinal studies [20, 95] and was significantly different between the two groups *(p=0.000).* In the (AP +) group, 21 cases were uncertain and in the (AP-) group, 7 uncertain treatments with inconstant symptoms which endodontic aetiology has not been confirmed, were observed before one year. 19.18 % of the teeth (AP-) were extracted *versus* 33.6 % of teeth (AP+). 6.85 % in the (AP-) group were re-treated *versus* 7.27 % in the (AP+) group. Moreover, the reasons of failure were different for each group. For AP-, recurrent tooth decay was responsible of failure for 31.7 %, widely before the periapical disease (19.5 %) and iatrogenic treatments (17 %). For (AP+), 1/3 of failure case was related to the development of apical periodontitis.

Significant differences were found for characteristic baseline *(tables 2)* between the two groups. **58%** (AP+) teeth were re-treated *versus* 26% (AP-) *(p=0.0000)*. **37%** (AP-) teeth were treated for prosthetic indication, without previous symptom (p=0.000). **35%** (AP-) teeth were treated with immediate filling *versus* **22%** (AP+) teeth *(p=0.022).*

79% % (AP-) teeth had a correct filling length *versus* **63%** (AP+) teeth *(p=0.009).*

A discrepancy between filling length and shaping length was recorded for **12%** (AP+) *versus* 3% (AP-) *(p=0.006).*

Over-filling was observed for **3%** (AP-) teeth *versus* **5%** (AP+) *(p=0.044)* and under-filling was found for **28%** (AP+) teeth *versus* **17%** (AP-) *(p=0.044).*

Survival of root canal treatments:

Failure occurs earlier for teeth with previous apical periodontitis: survival probability of endodontic therapy was about 75% after 21 months for (AP+) group *versus* 37 months for (AP-), and about 50% after 53 months for (AP+) group *versus* 93 months for (AP-).

After 108 months, survival probability of endodontic therapy was 24 % for the population with previous apical periodontitis (AP +) *versus* 37 % for the group without initial pathology *(graph 1).*

Teeth without previous apical periodontitis (AP-):

In (AP-) group, 2 cases with a survival time equal to 0 were deleted, and 144 were recorded for survival analysis. Failure treatments were observed between 0 and 108 months (9 years). The 1 year-survival probability was about 0.93. After 27 months, the survival probability decreased to 0.87. In other words, lower than 13% of the failed treatments occurred during the first 2 years. Half of failed treatments were recorded in 93 months *(graph 2).*

The reason of delayed failure in this group is essentially recurrent tooth decay linked to coronal leakage: 8 of 13 failed treatments for recurrent carious disease were observed between 27 and 93 months. The other reason of delayed failure was periodontal disease, observed at 108 months *(table 3a).*

Early failure is linked to iatrogenic procedures, and to the appearance of an apical radiolucency. 60% of failed treatments for iatrogenic etiology occurred during the first 6 months and 75% of failed treatments for apical periodontitis post-obturation were recorded during the first 3years.

In the monovariate analysis *(table 3b),* the log-rank tests showed that endodontic therapy failure was associated with a complex root canal anatomy *(p=0.035*), multirooted teeth *(p=0.015),* the presence of forgotten and additional root canals *(p=0.024),* the presence of calcifications *(p=0.010),* the absence of a definitive *(p=0.000)* and correct *(p=0.000)* coronal restoration, an iatrogenic treatment *(p=0.001)* with the presence of either pulpal floor perforations *(p=0.027)* either root perforations *(p=0.006),* or broken files *(p=0.000).* For a defective

coronal restoration with coronal leakage, the risk of failure was equal to 25.41. For an iatrogenic root canal treatment, the risk of failure was equal to 7 and increased to 19.13 with the presence of perforations.

Significant statistical interactions were observed between the variable *skill* and several others variables as *iatrogenic treatment, complex root canal anatomy, preparation technique* and *presence of severe root canal curvatures*. In consequence, the final Cox model was stratified on *Skill.*

The Cox model showed that the presence of forgotten and additional root canals *(p=0.000),* a provisional *(p=0.000)* and defective *(p=0.062)* coronal restoration, a stainless-steel hand files preparation *(p = 0.002)* and under-filling *(p = 0.007)* were statistically associated with failure of endodontic therapy for teeth without apical periodontitis *(cf table 4a).*

Teeth with previous apical periodontitis (AP+):

In (AP+) group, 5 cases with a survival time equal to 0 were deleted, and 105 were recorded for survival analysis. Failure treatments were observed between 0 and 111 months (9 years) *(graph 3).*

The 1 year-survival probability was about 0.809, with 19 failed treatments. After 21 months, the survival probability decreased to 0.756. In other words, about 25% of the failed treatments occurred during the first 2 years. Half of failed treatments were recorded in 53 months.

As the other group, the reason of delayed failure was essentially recurrent carie linked to a coronal leakage: 6 of 9 failed treatments for recurrent carious disease were observed between 24 and 97 months. The other reasons of delayed failure are either periodontal disease (observed at 108 months) or endo-periodontal pathologies (3/4 failure at 29, 63 and 111 months).

Early failure was linked to iatrogenic procedures and to the absence of periapical healing: failed treatments for iatrogenic etiology occurred during the first 4 months and more than 50% of failed treatments for enlargement of the periapical lesion were recorded during the first year, 77% during the first 2.5 years. Prosthetic indication and root fracture were also responsible for premature extractions *(table 3a).*

In the monovariate analysis, the log-rank tests showed that endodontic therapy failure was associated with the absence of a definitive *(p=0.000)* and correct *(p=0.006)* coronal restoration, a high initial Periapical Index (PAI) *(p=0.017*), the presence *(p=0.003)* and the size *(p=0.029)* of the apical radiolucency, a discrepancy between working length and filling length *(p=0.000) (table 3c).* For a defective coronal restoration with coronal leakage,

the risk of failure was equal to 29. For a provisional coronal restoration, the risk of failure was equal to 20.8. For a discrepancy between working length and filling length, the risk of failure was equal to 6.642 and for the obvious presence of apical radiolucency, the risk of failure was equal to 3.069.

The Cox model, stratified on *Skill* showed that the absence of a definitive *(p=0.000)* coronal restoration, the size of the apical radiolucency *(p=0.025),* a discrepancy between working length and filling length *(p=0.006),* the presence of forgotten and additional root canals *(p=0.088)* were statistically associated with absence of periapical healing and failure of endodontic therapy for teeth with previous apical periodontitis (table 4b).

Periapical Healing:

The first complete periapical healing was observed after 10 months. Periapical healing increased in time: successful cases were respectively 4%, 31.2% and 63.7% for a follow-up period of 1, 2 and 4 years. The main successful treatments were recorded during a recall period from 1 to 7 years. 50% of periapical healing occurred within 42 months and after 81 months, 24% of healing process was not achieved. Probability of failure or incomplete periapical healing was still 0.08 after 9 years. The last healed case was observed after 138 months (11.5 years) *(graph 4).*

In the monovariate analysis, the log-rank tests showed that periapical healing was improved with a Ni-Ti rotary preparation *(p=0.000),* a correct *(p=0.049)* and definitive coronal restoration *(p=0.009),* the absence of severe root canal curvature *(p=0.001),* the anterior localization of teeth *(p =0.018)* and a small sized apical radiolucency *(p=0.051) (table 3d).*

The Cox model highlighted 4 predictive factors of periapical healing: a definitive coronal restoration *(p = 0.017),* a Ni-Ti rotary preparation *(p=0.000),* the absence of severe root canal curvature *(p=0.042)* and a high grade of skill *(p = 0.025).*

However, significant statistical interactions between the co-variables *skill* and both *preparation technique* and *presence of severe root canal curvatures* were observed. In consequence, the final Cox model was stratified on *Skill* and conclude that a definitive coronal restoration *(p = 0.011),* a Ni-Ti rotary preparation *(p=0.000)* and a prosthetic indication of treatment *(p = 0.022)* were linked to periapical healing *(table 4c).*

Discussion

Population

In this longitudinal prospective cohort, 107 patients who had received endodontic treatments during a complex periodontal and occluso-prosthetic treatment were re-examined for long-term outcome. This population followed for a long global oral rehabilitation are faithful to the Dental Care Center at the Nantes University Hospital. In this way, we avoided low recall-rates which was one of the limitation of the assessment of root canal outcome [132], as reported by previous follow-up studies [58, 60, 66-71].

Moreover, to avoid supplementary appointments for the patients, we choose to assess the root canal treatments during their inter-disciplinary care. The assessment of endodontic outcome was performed at least one year after root canal filling (except for premature failure) and was repeated until the oral rehabilitation was totally achieved. Most of them have been seen during annual appointments. Patients receiving root canal treatments during emergency were excluded. The randomly recruitment allows to select a representative sample of this population treated for a long global oral rehabilitation at University Hospital of Nantes.

Design

This is a randomly clinical prospective study, including 256 treatments to have a powerful analysis for this study design (power >0.95). The studied population was selected over several years to be well-representative of both the clinical practice of the Endodontics department of Nantes University and the frequency of the pulpar and periapical diseases.

Many prognosis factors of endodontic treatment outcome had been described in the literature [19, 83, 84, 137, 142]. The purpose of this cohort was to assess the simultaneous influence of all these factors on the long-term survival of root canal treatment using a Cox Model. Other studies have proposed multivariate statistical analyses with logistic regression [58, 60, 63, 66-71], but much fewer with survival models [52, 59, 61, 62, 134]. Simple calculation of percentages does not provide sufficient information on root canal outcome [61]. Conclusions of logistic regression models do not reflect that the failure rate of endodontic therapy and the periapical healing can be variable over time. A wide proportion of healing cases were initiated and detectable after one year, but complete healing required 4 years for completion [53], Many authors recommended a longer follow-up period

[44-46, 52, 59, 61, 64, 99, 126, 127] based on results that had highlighted an increasing survival probability of healing beyond 4 years. In our clinical study, proportions of healed cases were respectively 4%, 31.2% and 63.7% for a follow-up period of 1, 2 and 4 years and after 81 months, 24% of healing process was not achieved. Furthermore, delayed failures were observed until 9 years. Patients without definitive status can seriously lead to misinterpretation of the results [61]. These problems are resolved by using statistical methods of survival analysis, censoring such intermediate situations or incomplete events, and taking into account the time of follow-up. Survival multivariate analysis was considered suitable for similar studies [56, 59, 61, 62, 95, 147]. Moreover, several survival analyses as Cox model were suggested for variable recall-periods [59], as observed in our prospective study.

Besides, a prospective assessment avoided missing data and was appropriate to collect precise and correct information about the initial disease, the indications of root canal treatment, as well as procedurals errors that may compromise the short or long-term outcome. In this study, we were also able to identify premature failures before root canal filling.

The preoperative periapical status appears to be one of more decisive factor for the outcome of endodontic treatment [44-47, 52, 56, 58, 59, 64, 66-68, 70, 71, 106]. On the assumption that prognosis factors might be different according to the initial disease, the statistical analysis was conducted by dividing the population into 2 different groups: teeth with initial apical periodontitis and teeth without such initial lesion. As previous survival analyses [59, 61, 62, 134] on the outcome of the endodontic therapy, we estimated the long-term survival of root canal treatment. In addition we managed to assess the occurrence of healing of periapical radiolucencies over time, using for analysis the *complete healed cases* as attempted events and right-censoring incomplete healing or failed cases.

Statistical unit

As previous studies [59, 66-68], we chose the tooth as the statistical unit. The endodontic treatment of a multi-rooted tooth is considered as a failure when a periapical lesion occurs on one of the roots. When the unit is the root, the influence of multi-rooted teeth in the sample might be overestimated.

Survival of endodontic therapy:

The mean follow-up period was respectively 5.5 years for the (AP-) group and 4.5 years for the (AP+) group. The follow-up period consisted in multiple appointments and reached 171 months.

At the end of our study, recorded successful treatments were **71.9**% on teeth without previous periapical disease, and **41.8%** on teeth with initial apical periodontitis. Although our results agreed with earlier findings showing a higher success rate on teeth without apical periodontitis [19, 22, 66, 103], they were lower than those reported in previous published longitudinal studies [22, 63, 66, 95, 134]. Except for Cheung et al [61] who have reported a failure rate reaching 44%, higher cumulative survival probabilities (csp) varying between 0.68 and 0.95 were observed in others longitudinal studies using survival analysis methods *(table 5)*.

We assume that the low successful results should be related to a low skill level. In this cohort, most of the treatments were performed by inexperienced students. Furthermore, the low recall rate and the absence of recording extractions and re-treatments as failure in many clinical studies may have contributed to the overestimation of successful outcomes of endodontic therapy [132]. Moreover, overestimated success rates may be related to the periapical index scoring system (PAI) [132] recommended to assess periapical health [74] and frequently used in the outcome of root canal treatments [66, 69, 133]. Indeed, in several studies [66, 69], scores 1 and 2 were considered as healed or successful cases , despite score 2 would reflect mild periapical inflammation [151] and apical periodontitis was recorded only for PAI≥ 3. In this present study, success was considered as a symptoms free and functional tooth, without any apical radiolucency and pathological periodontal ligament space.

Another factor can explain our lower results: we exhaustively took into account all the endodontic treatments, whether they were achieved or ended by tooth loss before root canal completion. Recurrent flare-ups or iatrogenic procedural errors as pulpal floor perforations responsible of untimely extractions were generally underestimated or forgotten in the assessment of the endodontic therapy.

In our prospective cohort, 10% of root canal treatments with iatrogenic procedural errors were observed. Iatrogenic treatments were the major cause of early failures. Indeed, the risk of failure was 7 times higher for iatrogenic treatments in the group AP- (Log Rank, p = 0.000), and of 2.428 times higher in the group AP+ (Log Rank, p = 0.119). Against all expectations and contrary to previously published conclusions [67-70], iatrogenic procedural errors however did not appear as a significant predictive factor, only because the survival analysis was performed after deletion of many cases with a survival time equal 0.

Besides, our survival analysis demonstrated that failure occurred earlier for teeth with previous apical periodontitis. The survival mean that was about 106 months for the teeth without preoperative periapical lesions,

decreased to 66 months for teeth with apical periodontitis. 25% of failed treatments were observed after 21 months for (AP+) group *versus* 37 months for (AP-), and about 50% after 53 months for (AP+) group *versus* 93 months for (AP-).As observed previously [62], the survival functions declined with time, with a drop in the first years after treatment. Our results showed a rapid decreasing survival before 4 years; the occurrence of failures appeared to slow down with a longer observation time.

Periapical Healing:

In this present study, we managed to assess the survival occurrence of complete healing events *e.g.* symptoms free and functional teeth, without any apical radiolucency and pathological periodontal ligament space. Previous studies may have contributed to the overestimation of periapical healing when reduced size of the existing radiolucency or decreased PAI score diagnosed by radiographs were considered as valuable signs of successful healing [132]. For this reason, we took account only treatments with a complete disappearance of initial apical periodontitis during recall appointments. The others were right-censored in our survival analysis.

The survival curve (Fig 2) shows that healing can be achieved many years after treatment, thus increasing the difficulty of endodontic outcome analysis with premature re-examinations.

The first complete periapical healing was observed after 10 months. The main successfull treatments were recorded during a recall period from 1 to 7 years. The probability that complete periapical healing will take place increased continuously with the length of the observation period [76].

Only 4% of completely healed cases were observed 1 year after treatment, and respectively 31.2% and 63.7% for follow-up periods of 2 and 4 years.

Half of periapical healing occurred within 42 months and, the probability of failure or incomplete periapical healing was still 0.08 after 9 years. The last healed case was observed after 138 months (11.5 years).

These results are in agreement with previous studies [55, 61, 88] with a healing process beyond a period of 4 years. Nevertheless, previous results reported that the likelihood of successful healing within an observation time of five years exceeded 90% [76] while it was about 70% in our study. Periapical healing rate observed in a recent 2 to 4 years follow-up study [63] was also higher that the 4 years-healing probability evaluated in this present study: ≥ 80% *versus* 63.7%. However, study designs and statistical analyses were different, over and above the fact that the recall rate was only 50%. Moreover, the simple calculation of success rates would overestimate the chance of complete periapical healing within the first years after therapy [95].

Survival analysis is suitable in order to take into consideration the individual observation times in assessing the prognosis of root canal treatment [95], This kind of analysis is particularly attractive to follow healing processes over a long period. The periapical healing was already studied by recording healed treated teeth as well as intermediate states of healing. Orstavik D in 1996 [105] concluded that 89 % of the initiated but incomplete periapical healing cases were observed 1 year after treatment. Now, the use of Cone Beam brings to light the limitations of the periapical radiographs in assessing the success of root canal treatment, especially based on incomplete healing [131, 132]. Cone Beam technique was not available at the beginning of this present prospective study. Moreover, the commonly use of Cone Beam in assessing the outcome of endodontic therapy in France is actually improbable.

For this reason, the obvious think to do in estimating long-term healing process by periapical radiographs was to record healed cases as the attempted event, *e.g. ad-integrum* repair of the periapical tissues. Any observation with residual periapical radiolucency, even if a bone remodeling process was seen, was considered as the *absence of healed treatment* and right-censored.

Predictive factors of endodontic outcome

Our Cox models showed that the lack of definitive coronal restoration or the imperfect, the provisional coronal restoration compromised the long-term success of endodontic treatment in both 2 groups.

Many papers have also concluded that the coronal leakage might be an essential prognosis factor in endodontics [83, 84, 107-110]. The Cox model performed for (AP +) showed that periapical healing seems to be improved by a sealed tight and definitive coronal restoration or core. The absence of a correct and definitive coronal restoration should considerably reduce both the survival period and the survival probability. For (AP-), the mean survival time recorded with a correct and definitive coronal restoration was 120 months (with a survival median= 108) and decreased to 34 months (with a survival median= 21) with a defective and provisional restoration. For the other group (AP+), the mean survival time dropped from 91 months (with a survival median=108) to 32 months (with a survival median= 21).

During and after the restoration of endodontically treated teeth, contamination of root canal can occurs and may result in delayed failures. Influences of microleakage and placement of provisional restorations on apical seal and periapical health have been reviewed [135] and the literature suggests that the outcome of endodontic therapy can be improved by an appropriate and prompt restoration after completion of root canal filling. Several authors [89, 108, 152] recommended a permanent restoration in order to prevent inadequate sealing and

minimize microleakage of bacteria and endotoxins [153, 154]. Although, our results were consistent with conclusions of several studies [63, 111, 130, 134], tooth loss is often the direct outcome of caries revival and not linked to an apical periodontitis. As suggested previously [111], the impact of the coronal leakage or the type of restoration on the endodontic outcome must be carefully analyzed in order to identify and spread any confounding factor.

Our Cox models showed that the outcome of endodontic therapy was altered by either an under-filling, either a forgotten root canals for the group (AP-), or a discrepancy between the working length and the filling extent for the group (AP+). It has been argued that the endodontic outcome was intimately linked to the quality of treatment performed [103]. The debate about the effect of the filling quality has been raised by many authors [24, 26, 28-31, 33, 39, 44-46, 48, 66-68, 90, 112, 122-125, 127]. Although several multivariate analysis confirmed this hypothesis [34, 52, 56, 59] and have reported a higher risk of failure with an incorrect filling extent of teeth with apical periodontitis [34, 44, 52, 60], others did not find any significant effect of the filling extent on failure of root canal treatment [60, 64, 66-68, 70, 71, 106].

Our final models are consistent with previous findings [58, 64, 66-68, 106, 128] that support that the major factors associated with endodontic failure are the persistence of bacterial infection in the canal space and/ or the periradicular area and the preoperative apical periodontitis. The apical extent of root canal treatment is partly responsible of the failure when linked to an incomplete elimination of microbes in infected root-canals or with a bacterial contamination.

Indeed, we were in accordance with several authors [63, 131, 134-137], concluding that the risk of failure increased with the association of a provisional or defective coronal restoration and an incorrect filling extent. Lower failure rates were observed for treated teeth with early definitive coronal restorations with high quality of the root canal fillings.

We have included the volume of the periapical radiolucency in our survival analysis to identify predictive failure factors of periapical healing. Our results showed that the size of lesions exerted a significant influence on endodontic outcome according to previous conclusions [58, 63].

We noticed that failure rate and survival time were conversely proportional to the magnitude of the lesion, except for one case which diameter was about 10mm. High volume of the perapical radiolucency didn't avoid healing but would increase the delay of healing completion. Moreover, a higher success rate for large lesions (10 mm^2 extent) has been reported [119]. Although periapical radiographs were used in most previous outcome

studies, the validity of using periapical radiographs to evaluate the healing process might be questionable [131, 132]. Recently, Cone Beam Computed Tomography has been introduced to the field of endodontics [155] and has highlighted the lack of sensivity of periapical radiographs in evaluating post-treatment periapical lesions [156-158].

Although all our periapical radiographs have been taken with the same model X-ray machine with a long cone paralleling technique and standard settings, the impact of the size of the lesion on endodontic outcome must be carefully analyzed according to the imprecision in measuring periapical lesion extent with such radiographic examination.

According to previous studies [46, 57, 65, 67, 68, 70, 71], the variable *preparation technique* seemed to be correlated to endodontic treatment outcome in our multivariate analysis.

In this prospective cohort, root canal shaping was equally performed with either a stainless-steel hand files technique or a Nickel-Titanium rotary files technique. The survival outcome of endodontic treatments was improved by using a rotary Ni-Ti instrumentation. Nevertheless, a strong correlation between the operators' grade and the shaping techniques was observed. The variable *"skill level"* was either significantly linked with the outcome and/or to other predictive variables. The skill factor was probably a confounding factor. In this cohort, colinearity was found between tooth localization (*anterior versus posterior*), complex root canal anatomy, preparation techniques and skill level because the most difficult treatments were usually allocated to postgraduate students and qualified endodontists and performed with Nickel-Titanium rotary files. For this reason, our Cox models were proposed with stratification on the variable *skill level*.

According to previous studies [46, 57, 65, 67-71], our final Cox models showed that root-canal therapy is technique–sensitive. The use of Nickel-Titanium rotary files is effective in reducing intra-canal bacteria and endotoxins by optimizing root canal chemo-mechanical preparation, irrigation and disinfection of the apical third and will enhance the successful outcome of endodontic therapy [139, 145, 159, 160].

Clinicians know that re-treatment is a difficult procedure which outcome largely depends on the complexity of root canal morphology and the presence of preoperative apical periodontitis. Several authors [44] have suggested that re-treatment appears to be decisive for the outcome of endodontic treatment, but others did not support this hypothesis [58, 59, 63, 126, 134] and this tallies with our results. Moreover, some meta-analyses have reported no different estimated pooled success rates for both initial and secondary root canal treatments [83, 84, 107].

Surprisingly, our survival model showed that prosthetic indication to treat teeth with initial apical periodontitis was a significant positive prognosis factor in periapical healing *(table 6).* In this prospective study, the indication of root canal treatments was exactly recorded. The treatments were undertaken either in presence of acute or chronic pulpar and periapical diseases or for prosthetic reasons. 13 teeth treated for prosthetic reason had a doubtful periapical health with a widened periodontal ligament. Only 2 of them presented a PAI score= 3. All these treatments realized for prosthetic reason were in fact re-treatments. Although the monovariate analysis didn't show significant difference between teeth treated for prosthetic reason and those treated for pathological reasons, a higher periapical healing rate (0.615 *vs* 0.413) and a lower failure rate (0.077 *vs* 0.402) were observed in the group of teeth (AP+) re-treated for prosthetic reason. This population consists of treatments that were recommended for a supposed apical periodontitis and not for really and obvious failed initial treatments. Moreover, these teeth were allocated to the (AP+) group based on a periapical radiographic examination which might be responsible of an erroneous initial diagnosis.

Conclusions:

This prospective cohort shows high survival probabilities 1 year after root canal treatment completion: 93% for teeth with no preoperative periapical pathology, and 83% for teeth with initial apical periodontitis. Survival decreases with time, with a rapid drop before 4 years after treatment: survival probabilities for teeth with no preoperative periapical pathology are 65% after 4 years, and about 55% for teeth with initial apical periodontitis. The occurrence of failures appeared to slow down with a longer observation time. Besides, failure occurs earlier for teeth with previous apical periodontitis.

The probability of periapical healing is lower than 4% before 1 year and increases to 63.7% for a follow-up period of 4 years. After 81 months, 24% of healing process was not achieved and this underlines the difficulty of assessment of the outcome of root canal therapy. Survival analysis is suitable to bring to light the periapical healing time varying from 10 to 138 months (11.5 years), period within all successful healings with complete repair of the periapical radiolucency are observed.

The results of this prospective cohort suggest that periods of revaluation according to consensus on quality guidelines [117, 118] could be undersized to be able to predict the long-term outcome of endodontic therapy. This study has laid emphasis on the fact that periapical healing is a long and delicate process and may require a follow-up for over 4 years.

However, there are recurrent factors associated with the survival of endodontic treatments. Our survival model shows that a defective endodontic obturation in association with a coronal leakage is a significant negative prognosis factor in outcome of root canal treatments. These findings support the fact that the complete disinfection and filling of root canal space followed by a prompt and definitive coronal restoration is the core concept of the success of endodontic therapy.

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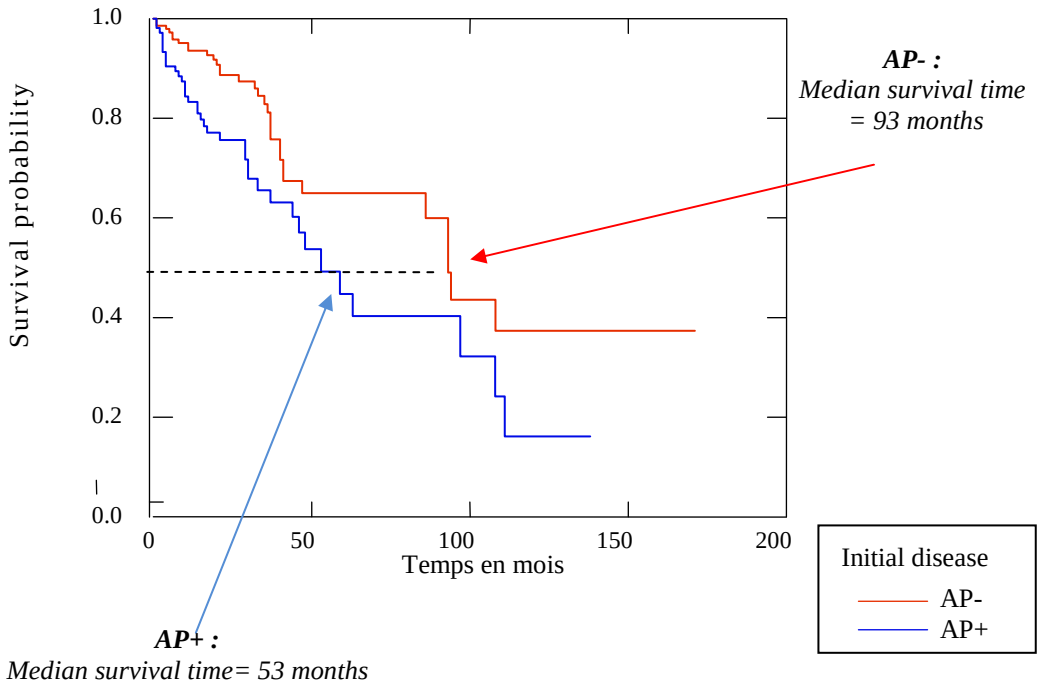
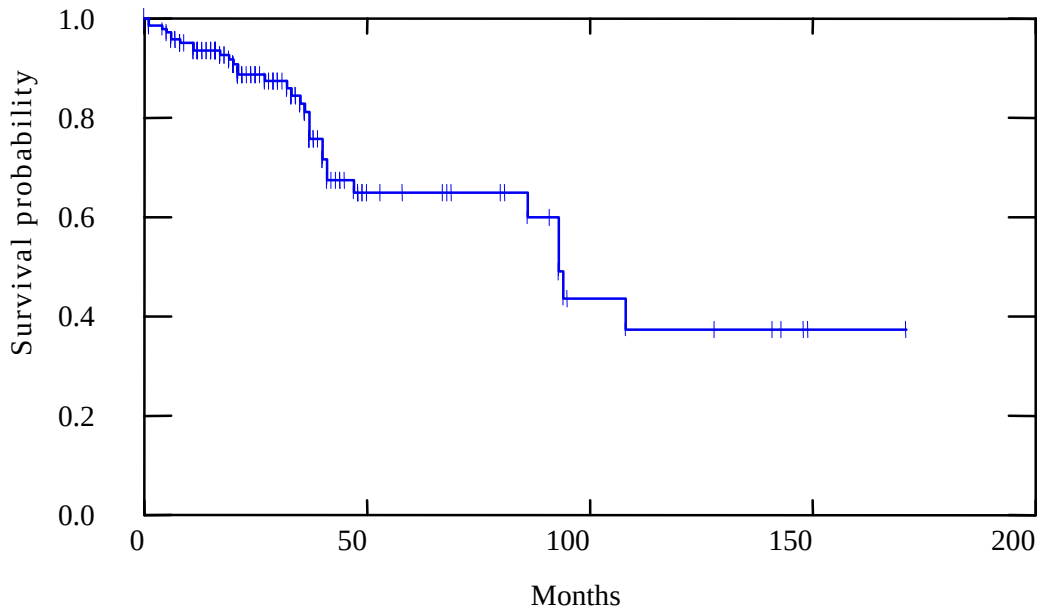
Graph 1: Occurrence of the endodontic therapy failure over the time in teeth with (AP+) or without initial apical periodontitis (AP-)



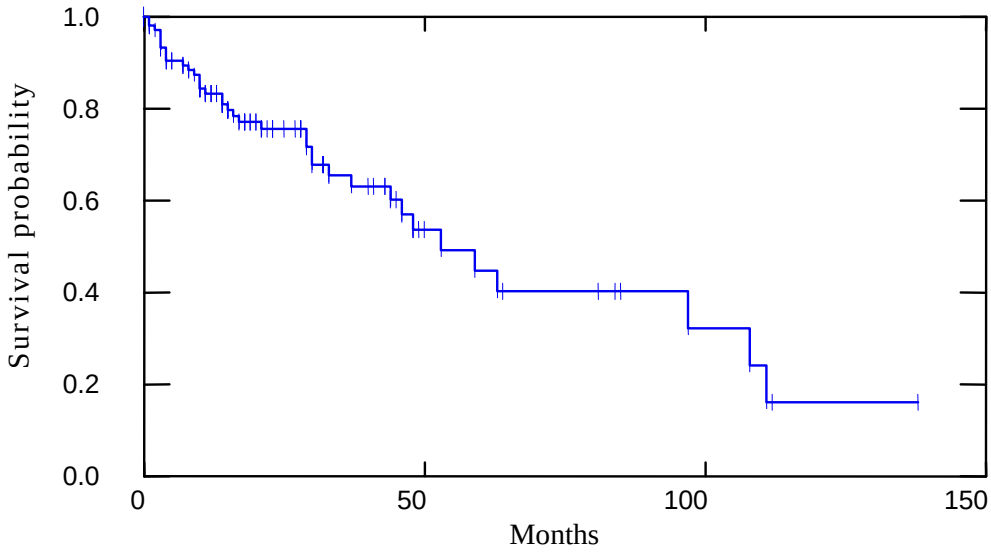
	Group (AP-) N = 144	Group (AP+) N = 105
Number of failures	*32*	*38*
Mean survival time	*106 months*	*66 months*
Survival quantiles	*76% à 37 months*	*76% à 21 months*
	49% à 93 months	*49% à 53 months*
	37% à 108 months	*24% à 108 months*

Graph 2: Occurrence of failure of the treated teeth without previous apical periodontitis (AP-)



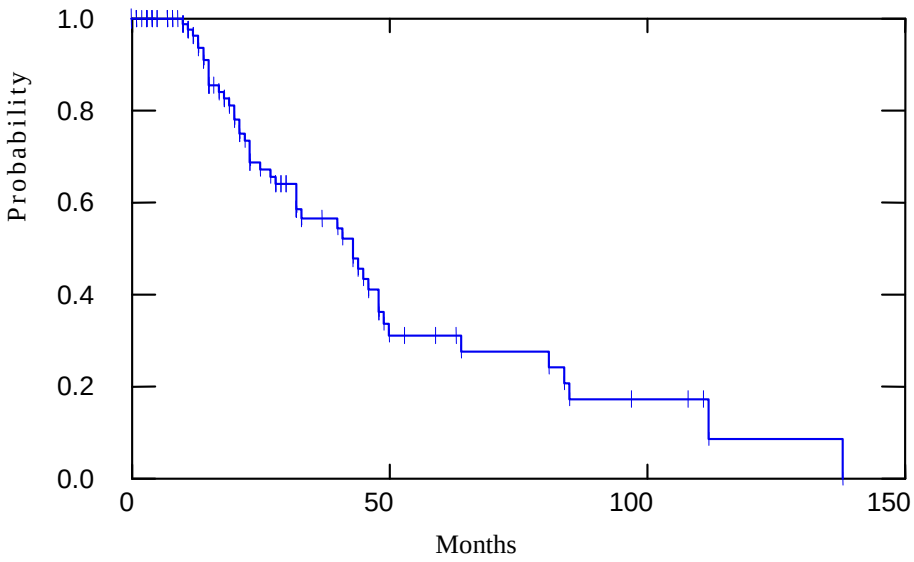
Survival curve: *the survival probability decreases from 0 to 108 months, period during which all the failure cases are observed.*

Graph 3: Occurrence of failure of the treated teeth with previous apical periodontitis (AP+)



Survival curve: *the survival probability decreases from 0 to 111 months, period during which all the failure cases are observed.*

Graph 4: occurrence of the complete periapical healing over the time



Survival curve: *the probability of absent or incomplete periapical healing decreases from to 10 à 138 months, period during which all the healed cases are observed.*

N = 105

Number of successfull healing cases = *46*
Mean of healing time= *53 months*

Quantiles :
75% *21 months*
48% *43 months*
24% *81 months*

Table 1a: Estimation of quantitative variables related to the follow-up of root canal treatment in the 2 groups.

	Follow-up period (months)		**Number of re-examination appointments**	
	AP-	**AP+**	**AP-**	**AP+**
N	146	110	146	110
Minimum	0(*)	0(*)	0(*)	0(*)
Maximum	171	138	6	5
Mean	24.5	27	2.185	1.9
Median	34.2	18.5	2	2
Standard deviation	31.7	26.56	1.083	0.888

LILLIEFORS test, p >0.05: the quantitative variables are normal.

(*) *immediate therapeutic failures*

Table 1b: Outcome of root canal treatments at the end of the prospective study (July 2011) and etiology of failure (estimation by frequencies and percentages).

	AP- ***N=146***		***AP+*** ***N= 110***		***Chi²*** ***p-value***	***All the population*** ***N=256***	
	n	***%***	***n***	***%***		***n***	***%***
Outcome of root canal treatment					***0.000***		
Success	*105*	*71.918*	*46*	*41.818*		*151*	*58.984*
Incertain cases	*7*	*4.795*	*21*	*19.091*		*28*	*10.938*
Failure	*34*	*23.288*	*43*	*39.091*		*77*	*30.078*
Therapeutic decision					***0.027***		
Abstention	*108*	*73.973*	*65*	*59.091*		*173*	*67.578*
Re-treatment	*10*	*6.849*	*8*	*7.273*		*18*	*7.031*
Extraction	*28*	*19.178*	*37*	*33.636*		*65*	*25.391*
Etiology of failure (tooth loss and re-treatment)					*0.152*		
Recurrent carious disease	*13*	*31.707*	*9*	*20*		*22*	*25.581*
Iatrogenic procedure	*7*	*17.073*	*4*	*8.89*		*11*	*12.791*
Apical periodontitis	*8*	*19.512*	*15*	*33.3*		*23*	*26.744*
Endo-periodontal lesion	*2*	*4.878*	*5*	*11.1*		*5*	*5.814*
Root canal fracture	*3*	*7.317*	*3*	*6.67*		*5*	*5.814*
Periodontal pathology	*3*	*7.317*	***5***	*11.1*		*8*	*9.302*
Prosthetic indication	*5*	*12.195*	*2*	*4.4*		*5*	*5.814*
Not recorded			*2*	*4.4*		*7*	*8.140*

Chi^2 test, $p \leq 0.05$:significative

Tables 2 : Characteristic baseline.

***Table 2a**: Distribution of factors related to the tooth (values expressed in frequencies and percentages)*

	AP- ***N=146***		***AP+*** ***N= 110***		***Chi²*** ***p-value***	***All the population*** ***N=256***	
	n	***%***	***n***	***%***		***n***	***%***
Localization in mouth							
maxillar	*74*	*51 %*	*67*	*61 %*		*145*	*55 %*
mandibular	*71*	*49 %*	*43*	*39 %*	*0.189*	*115*	*46 %*
anterior	*49*	*34 %*	*45*	*41 %*		*109*	*59 %*
posterior	*97*	*66 %*	*55*	*59 %*	*0.227*	*76*	*41 %*
Tooth type							
single-rooted	*76*	*52 %*	*55*	*50 %*		*131*	*51 %*
multi-rooted	*70*	*48 %*	*55*	*50 %*	*0.745*	*125*	*49 %*
Complex root canal anatomy							
absence	*108*	*74 %*	*83*	*75 %*		*191*	*75 %*
presence	*38*	*26 %*	*27*	*25 %*	*0.787*	*65*	*25%*
Intracanal calcification/obliteration							
absence	*122*	*84 %*	*91*	*83 %*		*213*	*83 %*
presence	*24*	*16 %*	*19*	*17 %*	*0.860*	*43*	*17%*
Curvature							
absente ou not significative	*136*	*93 %*	*107*	*97 %*		*243*	*95 %*
severe	*10*	*7 %*	*3*	*3 %*	*0.137*	*13*	*5 %*

3

***Table 2b**: Distribution of factors related to initial pathological situation (values expressed in frequencies and percentages)*

	AP- ***N=146***		***AP+*** ***N= 110***		***Chi²*** ***p-value***	***All the population*** ***N=256***	
	n	***%***	***n***	***%***		***n***	***%***
Acute pathology							
absence	*83*	*57 %*	*85*	*77 %*		*252*	*98 %*
presence	*63*	*43 %*	*25*	*23 %*	***0.001***	*4*	*2 %*
Apical periodontitis							
absence	*146*	*100 %*	*54*	*49 %*		*200*	*78 %*
presence	*0*	*0 %*	*56*	*51 %*	***0.001***	*56*	*22 %*
Size of the periapical radiolucency							
≤ 1mm			*25*	*45 %*			*10 %*
1 <s≤ 3mm			*22*	*39 %*			*9 %*
3 <s≤ 5mm			*3*	*5 %*			*1 %*
> 5mm			*6*	*11 %*	***0.000***		*2 %*
Traumatism							
absence	*144*	*99 %*	*108*	*98 %*		*252*	*98 %*
presence	*2*	*1 %*	*2*	*2 %*	*0.775*	*4*	*2 %*
Endo-periodontal lesion							
absence	*146*	*100 %*	*106*	*96 %*		*154*	*60 %*
présence	*0*	*0 %*	*4*	*4 %*	***0.020***	*102*	*40 %*

***Table 2c**: Distribution of factor related to the procedures of treatment and the skill level of the operator (values expressed in frequencies and percentages)*

	AP- **N=146**		***AP+*** ***N= 110***		***Chi²*** ***p-value***	***All the population*** ***N=256***	
	n	***%***	***n***	***%***			
Skill level					*0.364*		
Qualified endodontits	*3*	*2 %*	*6*	*6 %*		*9*	*3%*
Interns, postgraduate students	*29*	*23 %*	*21*	*21 %*		*50*	*20%*
Undergraduate students	*98*	*75 %*	*74*	*73 %*		*172*	*67 %*
unrecorded						*25*	*10%*
Re-treatment							
absence (initial treatment)	*108*	*74 %*	*46*	*42 %*		*154*	*60 %*
presence	*38*	*26 %*	*64*	*58 %*	***0.000***	*102*	*40 %*
Prosthetic indication							
absence	*92*	*63 %*	*96*	*87 %*		*154*	*60 %*
presencei	*54*	*37 %*	*14*	*13 %*	***0.000***	*102*	*40 %*
Technique of root canal preparation							
Stainless steel hand files	*66*	*47 %*	*54*	*52 %*		*120*	*49 %*
Nickel-titanium rotary files	*75*	*53 %*	*49*	*48 %*	*0.386*	*124*	*51 %*
Technique of root canal filling							
Lateral condensation of GP	*125*	*90 %*	*89*	*90 %*		*232*	*91 %*
Warmed GP	*14*	*10 %*	*10*	*10 %*	*0.994*	*24*	*9 %*
Inter-appointement medication							
none	*47*	*32 %*	*21*	*19 %*		*68*	*27 %*
Calcium hydroxide	*93*	*64%*	*87*	*79 %*		*180*	*70 %*
other	*6*	*4 %*	*2*	*2 %*	***0.026***	*8*	*3 %*
Number of visits							
Immediate filling	*51*	*35%*	*24*	*22 %*		*75*	*29 %*
) 1	*95*	*65 %*	*86*	*88 %*	***0.022***	*181*	*71 %*

***Table 2d**: Distribution of factor related to the quality of root canal treatment and the coronal restoration (values expressed in frequencies and percentages)*

	AP- ***N=146***		***AP+*** ***N= 110***		***Chi²*** ***p-value***	***All the population*** ***N=256***	
	n	***%***	***n***	***%***		***n***	***%***
Iatrogenic procedures							
absence	*135*	*92 %*	*95*	*86 %*		*230*	*90 %*
presence	*11*	*8 %*	*15*	*14 %*	*0.110*	*26*	*10 %*
Filling extent							
correct	*110*	*79 %*	*64*	*63 %*		*174*	*68%*
incorrect or absent	*30*	*31 %*	*37*	*37 %*	***0.009***	*67*	*32 %*
Correspondance between instrumentation length and filling length							
correct	*134*	*97%*	*89*	*88 %*		*223*	*87.5 %*
incorrect	*4*	*3 %*	*12*	*12 %*	***0.006***	*16*	*6 %*
Over-filling (> radiographic apex)							
absence	*150*	*97 %*	*97*	*95 %*		*247*	*96.5 %*
presence	*4*	*3 %*	*5*	*5 %*	***0.044***	*9*	*3.5%*
Under-filling (≥ 2 mm before the radiographic apex)							
absence	*127*	*83 %*	*74*	*72 %*		*201*	*79%*
presence	*26*	*17 %*	*29*	*28 %*	***0.044***	*55*	*21 %*
Quality of the coronal restoration							
correct	*125*	*90 %*	*90*	*88 %*		*215*	*83 %*
defective or absente	*13*	*11 %*	*12*	*12 %*	*0.964*	*45*	*17 %*
Type of coronal restoration							
definitive	*114*	*82 %*	*77*	*77 %*		*191*	*80 %*
provisional	*25*	*18 %*	*24*	*24%*	*0.273*	*49*	*20 %*

***Tableau 2e**: Distribution of factors related to iatrogenic and error procedures (values expressed in frequencies and percentages)*

	AP- ***N=146***		***AP+*** ***N= 110***		***Chi²*** ***p-value***	***All the population*** ***N=256***	
	n	***%***	***n***	***%***		***n***	***%***
Perforations of the pulpal floor							
absence	*140*	*96 %*	*108*	*98 %*		*248*	*97 %*
presence	*6*	*4 %*	*2*	*2 %*	*0.887*	*8*	*3 %*
Root cracks							
absence	*146*	*100 %*	*109*	*99 %*		*255*	*99 %*
presence	*0*	*0 %*	*1*	*1%*	*0.278*	*1*	*1%*
Root perforations							
absence	*144*	*99 %*	*105*	*95 %*	*0.748*	*249*	*97 %*
presence	*2*	*1 %*	*5*	*5%*		*7*	*3 %*
Broken files							
absence	*145*	*99 %*	*106*	*96 %*		*251*	*98 %*
presence	*1*	*1 %*	*4*	*4%*	*0.218*	*5*	*2 %*
Intra canal ledges and abutments							
absence	*144*	*99 %*	*107*	*97 %*		*251*	*98 %*
presence	*2*	*1 %*	*3*	*3 %*	*0.748*	*5*	*2 %*

Reasons of failure	AP-						AP+					
	N = 34	Survival time *(months)*			Survival quantiles		N = 36	Survival time *(months)*			Survival quantiles	
		MEAN	MIN	MAX				MEAN	MIN	MAX		
Carious disease	*13*	*32*	*6*	*93*	*77%* *54%* *23%*	*19 months* *27 months* *37 months*	*9*	34	*3*	*97*	78% 44% 22%	15 *months* 30 *months* 37 *months*
Apical periodontitis	*8*	*34*	*1*	*94*	*75%* *50%* *25%*	*8 months* *17 months* *36 months*	*13*	20	*1*	*59*	69% 54% 23%	3 *months* 11 *months* 30 *months*
Iatrogenic procedures	*5*	*19*	*1*	*47*	*80%* *40%* *20%*	*1 months* *6 months* *37 months*	*2*	3.5	*3*	*4*	50%	3 *months*
Periodontal disease	*3*	*88*	*12*	*108*	*67%* *0%*	*12 months* *108 months*	*4*	49	*1*	*108*	80% 40%	1 *months* 21 *months*
Prosthetic indication	*3*	*35*	*5*	*50*	*67%* *33%*	*5 months* *49 months*	*2*	8.5	*7*	*10*	50%	7 *months*
Root fracture	*2*	*40*	*40*	*40*	*0%*	*40 months*	*2*	6.5	*4*	*9*	50%	4 *months*
Endo-periodontal lesion							*4*	59	*4*	*111*	80% 60% 30%	4 *months* 29 *months* 63 *months*

Table 3a: Reasons of failure in each group.

Table 3b: Monovariate analysis of predictive factors linked to the *failure* of treated teeth without initial periapical disease (AP-).

Factors	Relative risk (RR)	Statistic test: Log Rank		
		Value	df	Probability
Maxillar or mandibular localization	*0.904*	*0.359*	*1*	*0.549*
Anterior or posterior localization	*0.765*	*0.048*	*1*	*0.826*
Complex root canal anatomy	***1.826***	*4.450*	*1*	***0.035***
Number of root canals		*10.457*	*3*	***0.015***
Single rooted or multiple rooted tooth	*1.771*	*3.255*	*1*	*0.071*
Curvature	*0.347*	*1.790*	*1*	*0.181*
Calcification	***2.328***	*6.604*	*1*	***0.010***
Additional or forgotten canal	***5.23***	*5.090*	*1*	***0.024***
Acute disease	***1.958***	*1.111*	*1*	*0.292*
Prosthetic indication	*0.536*	*1.898*	*1*	*0.168*
Traumatism	*3.364*	*0.533*	*1*	*0.465*
Re-treatment	*0.413*	*0.994*	*1*	*0.319*
Skill level		*2.514*	*2*	*0.285*
Correspondence between filling length and shaping length	***4.154***	*0.100*	*1*	*0.752*
Quality of root canal filling	*1*	*0.785*	*1*	*0.376*
Over filling	*1.298*	*0.004*	*1*	*0.952*
Under filling	*0.903*	*0.956*	*2*	*0.620*
Quality of coronal restoration	***25.412***	*19.575*	*1*	***0.000***
Type of coronal restoration	***0.093***	*51.724*	*1*	***0.000***
Technique of root canal preparation	*0.780*	*0.052*	*1*	*0.819*
Technique of root canal filling	*0.667*	*0.270*	*1*	*0.603*
Immediate filling	*1.429*	*0.376*	*1*	*0.540*
Iatrogenic procedures	***7***	*11.656*	*1*	***0.001***
Perforation of pulpal floor	***19.138***	*4.910*	*1*	***0.027***
Root perforation	***0.810***	*7.532*	*1*	***0.006***
Broken files	***3.317***	*21.315*	*1*	***0.000***
Inter-appointement medication		*1.753*	*3*	*0.625*

$p \leq 0.05$: significative links

Table 3c: Monovariate analysis of predictive factors linked to the *failure* of treated teeth with apical periodontitis (AP+).

Factors	Relative risk (RR)	Statistic test: Log Rank		
		Value	df	Probability
Maxillar or mandibular localization	*1.418*	*0.787*	*1*	*0.375*
Anterior or posterior localization	*0.685*	*0.447*	*1*	*0.504*
Complex root canal anatomy	*1.096*	*0.505*	*1*	*0.477*
Number of root canals		*0.351*	*3*	*0.314*
Single rooted or multiple rooted tooth	*1.467*	*2.340*	*1*	*0.126*
Curvature	*0.774*	*0.414*	*1*	*0.520*
Calcification	*0.674*	*0.227*	*1*	*0.634*
Additional or forgotten canal	*1.571*	*2.708*	*1*	*0.1*
PAI		*8.192*	*2*	***0.017***
Acute disease	*0.844*	*0.001*	*1*	*0.988*
Prosthetic indication	*0.224*	*5.156*	*1*	*0.023*
Traumatism		*0.427*	*1*	*0.514*
Endo- periodontal disease	*1.584*	*0.222*	*1*	*0.637*
Periapical periodontis	***3.069***	*8.732*	*1*	***0.003***
Size of the periapical radiolucency		*15.647*	*7*	***0.029***
Retreatment	*0.624*	*1.687*	*1*	*0.194*
Skill level		*1.632*	*2*	*0.442*
Correspondence between filling length and shaping length	***6.642***	*16.911*	*1*	***0.000***
Quality of root canal filling	*1.034*	*0.769*	*1*	*0.380*
Over filling	*1.232*	*1.407*	*1*	*0.236*
Under filling	*0.942*	*0.184*	*2*	*0.668*
Quality of coronal restoration	***20.8***	*7.689*	*1*	***0.006***
Type of coronal restoration	***29.189***	*21.245*	*1*	***0.000***
Technique of root canal preparation	*6.642*	*0.893*	*1*	*0.345*
Immediate filling	*1.147*	*0.069*	*1*	*0.793*
Iatrogenic procedures	*2.691*	*2.428*	*1*	*0.119*
Perforation of pulpal floor		*0.839*	*1*	*0.360*
Root perforation	*1.041*	*1.540*	*1*	*0.215*
Broken files		*0.131*	*1*	*0.718*
Inter-appointement medication		*1.7377*	*2*	*0.420*

$p \leq 0.05$: significative link

Table 3d: Monovariate analysis of predictive factors linked to the *periapical healing* of treated teeth with apical periodontitis (AP+).

Factors	Relative risk (RR)	Statistic test: Log Rank		
		Value	df	Probability
Maxillar or mandibular localization	*0.528*	*0.389*	*1*	*0.533*
Anterior or posterior localization	***1.327***	*5.597*	*1*	***0.018***
Complex root canal anatomy	*1.153*	*3.540*	*1*	*0.060*
Number of root canals		*5.641*	*3*	*0.130*
Single rooted or multiple rooted tooth	*0.741*	*2.085*	*1*	*0.149*
Curvature	***2.864***	*10.641*	*1*	***0.001***
Calcification	*1.314*	*2.003*	*1*	*0.157*
Additional or forgotten canal	*1.4*	*0.569*	*1*	*0.451*
PAI		*5.081*	*2*	*0.079*
Acute disease	*0.730*	*1.403*	*1*	*0.236*
Prosthetic indication	*2.035*	*1.001*	*1*	*0.317*
Traumatism		*1.524*	*1*	*0.217*
Endo- periodontal disease	*1.585*	*2.732*	*1*	*0.098*
Size of the periapical radiolucency		*9.452*	*4*	***0.051***
Re-treatment	*1.210*	*0.717*	*1*	*0.397*
Skill level		*0.591*	*2*	*0.744*
Correspondence between filling length and shaping length	*0.205*	*0.008*	*1*	*0.930*
Quality of root canal filling	*0.726*	*1.178*	*1*	*0.278*
Over filling	*0.758*	*0.049*	*1*	*0.825*
Under filling	*0.911*	*2.260*	*1*	*0.133*
Quality of coronal restoration	***0.125***	*3.886*	*1*	***0.049***
Type of coronal restoration	***14.667***	*6.911*	*1*	***0.009***
Technique of root canal preparation	***1.287***	*25.165*	*1*	***0.000***
Immediate filling	*0.632*	*1.180*	*1*	*0.277*
Iatrogenic procedures	*0.459*	*0.092*	*1*	*0.762*
Lateral perforation	*0.333*	*0.026*	*1*	*0.872*
Broken files	*0.452*	*0.660*	*1*	*0.417*
Inter-appointement medication		*4.007*	*2*	*0.135*

$p \leq 0.05$: significative link

Tables 4 Multivariate analysis and final Cox models

Table 4 a*:* predictive factors linked to the *failure* of treated teeth without apical periodontitis (AP-).

	p- value
Single rooted canal or multiple rooted canal tooth	0.100
Additional or forgotten canal	**0.000**
Under filling	**0.007**
Quality of coronal restoration	0.062
Type of coronal restoration	**0.000**
Technique of root canal preparation	**0.002**

Table 4 b*:* Predictive factors linked to the *failure* of treated teeth with apical periodontitis (AP+).

	p-value
Size of the periapical radiolucency	**0.025**
Correspondence between filling length and shaping length	**0.006**
Type of coronal restoration	**0.000**
Additional or forgotten canal	0.088

Table 4 c*:* Predictive factors linked to the *periapical healing*

	p-value
Type of coronal restoration	**0.017**
Technique of root canal preparation	**0.000**
Severe curvature	**0.042**
Prosthetic indication	0.071
Skill level	**0.025**
Anterior or posterior localization	0.066

Authors	Study	Follow-up period	N	Recall rate	Survival	
Ng YL et al 2011	P	*2 to 4-years*	*759* initial treatments *858* re-treatments	*50%*	Initial treatment: Csp=*0.954 (0.936-0.968)* Re-treatments: Csp= *0.9543 (0.936-0.965)*	
Fonzar F et al 2009	R	*10 years*	*704* initial treatments *471* re-treatments	*75.2% patients*	Csp=*0.93*	
Cheung G 2002	R	*74 months ±34* Mean observation period *= 6.2 years*	*251*	73%	Failure rate = *44%* Median survival time = *113 months* Mean survival time = *91 months*	
Cheung et Chan 2003	R, r	*10 to 20 years*	*606*	52%	Median survival time = *111 months*	
Stoll et al 2005	R	*10 years* Mean observation period *= 33.7 months*	*914*		Csp= *0.74* Last loss=*106 months* Mean survival time = *104 months*	
Present study	P, r	*1 to 14 years* Mean observation period: **AP-:** *27 ±26.56 months* **AP+:** *34.2 ±31.7 months*	*256* *146* AP- *120* AP+	*100%*	**For AP-** At 1 year-: Csp = *0.93* At 93 months, Csp = *0.49* Mean survival time = *106 months* Last failure = *108 months*, Csp = *0.374* Failure rate = *23%*	**For AP+** At 1 year- Csp = *0809* At 108 months, Csp = *0.242* Mean survival time = *66 months* Last failure = *111 months*, Csp = *0.199* Failure rate = *39%*

Table 5: Survival outcome of root canal treatments; comparison of previously published results with those of this present study, based on survival analyses. *Study: R = retrospective, P = prospective, r = randomly selection of patients. Csp= cumulative survival probability.*

Treatments indicated for prosthetic reasons N=13						
0utcome	Complete healing N=8		Incomplete healing N=4		Failed healing N=1	
Initial periapical health	**Doubtful N=8**	Radiolucency N=0	**Doubtful N=2**	**Radiolucency** N=2	**Doubtful** N=1	**Radiolucency** N=0
Survival quantiles	Healing rate=0.615 Mean survival time=55 months 75%: 32 months 45%: 48 months 30%: 49 months				Failure rate=0.077 Mean survival time=122 months 83%: 44 months	

Treatments indicated for pathological reasons N=92						
0utcome	Complete healing N=38		Incomplete healing N=17		Failed healing N=37	
Initial periapical health	**Doubtful** N=24	**Radiolucency** N=14	**Doubtful** N=6	**Radiolucency** N=11	**Doubtful** N=12	**Radiolucency** N=29
Survival quantiles	Healing rate=0.413 Mean survival time=51 months 75%: 20 months 51%: 40 months 26%: 81 months				Failure rate=0.402 Mean survival time=57 months 75%: 16 months 49%: 48 months 27%: 97 months	

Table 6: Survival outcome of treatments undertaken for prosthetic reasons compared to this of treatments indicated for pathological reasons .

Conclusion

Il est essentiel de comprendre quels sont les facteurs qui favorisent ou qui pénalisent le succès de la thérapeutique endodontique. Notre travail avait comme objectif l'identification de facteurs prédictifs des traitements réalisés au Centre de Soins Dentaires afin de comprendre les déterminants de l'échec endodontique et de savoir dans quelle mesure les biomatériaux pourraient améliorer le pronostique de ces traitements. Comme la littérature et les différents travaux publiés dans ce domaine, nos 2 cohortes ont mis en évidence l'importance de la pathologie initiale, ainsi que la qualité de préparation et d'obturation canalaire, associée à une restauration ou reconstitution corono-radiculaire précoce et définitive. Ces résultats mettent en exergue la clé de voute du succès des thérapeutiques endodontiques : **la prévention et/ou l'éradication per et post opératoire de toute contamination bactérienne.**

Avec une pulpe vitale, la colonisation bactérienne (liée à la maladie carieuse en général) n'atteint pas le tiers apical, les tubulis dentinaires ou toute ramification endocanalaire [14]. Mais l'association d'une perte d'étanchéité coronaire à une obturation endodontique dont la condensation est insuffisante ou en sous-obturation serait une cause d'échec à long terme. Pour les dents ayant une pathologie périapicale initiale, le tiers apical est infecté [148, 161]. Dans ce cas, l'absence ou l'insuffisance de désinfection et d'instrumentation dans la portion apicale du canal peut compromettre la cicatrisation périapicale ; c'est par exemple le cas des dents avec une morphologie complexe et des courbures canalaires sévères [69, 72, 107, 156].

Il est indéniable que les efforts technologiques pour le développement de l'instrumentation Nickel-Titane ont contribué largement à optimiser l'ampliation de canaux courbes. De même, la préparation des canaux avec une conicité majorée a facilité l'irrigation de la portion apicale de l'endodonte [139, 145].

Néanmoins, la décontamination totale de celui-ci n'est pas encore assurée (de manière reproductible) avec les préparations canalaires par rotation continue et les irrigants actuels [162-165].

Quelle est la place des biomatériaux dans ce contexte ?

Il y a quelques décennies, le développement de biomatériaux en dentisterie était axé sur leur capacité à induire ou à favoriser la formation de tissus durs minéralisés. Ce type de biomatériaux a montré son efficacité dans de multiples indications : pour le coiffage direct, la réparation de perforations et de faux canaux en endodontie, la réalisation de barrières apicales lors d'apexification, l'apexogénèse ou encore comme matériau d'obturation a retro [102, 166-171].

Depuis quelques années, les recherches s'orientent plutôt vers le tissu engineering. La revascularisation et le rétablissement d'une pulpe vivante et fonctionnelle font l'objet de plusieurs travaux [170, 172-175].

La nanotechnologie est également explorée dans ce domaine. Les trames initialement utilisées en tissue-engineering étaient des matériaux biodégradables macroporeux ; les récentes recherches privilégient les nano structures proches de la matrice extracellulaire, afin de mieux contrôler la libération de molécules actives et le comportement cellulaire [176].

Cependant, si l'endodontie régénérative est une perspective plutôt séduisante, subsiste encore l'épineux problème de la désinfection bactérienne qui reste le talon d'Achille de la thérapeutique endocanalaire [177]. Comme pour les thérapeutiques endodontiques conventionnelles, le succès des procédures de régénération pulpaire dépendra d'une désinfection optimale du réseau endodontique et des tubulis dentinaires. Cependant, l'utilisation de nos irrigants canalaires peuvent modifier la structure des parois dentinaires et la capacité à promouvoir la régénération pulpaire.

Depuis peu, des solutions pour l'amélioration de la décontamination canalaire sont étudiées, notamment grâce au LASER [178-185] et à la nanotechnologie [186-190].

Les travaux réalisés actuellement évaluent l'efficacité de différents systèmes de libération de molécules actives sur le biofilm. **Ces nouvelles procédures de traitement pourraient changer radicalement l'endodontie dans la mesure où elles permettront la désinfection complète et ciblée du réseau endodontique.**

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Annexes :

- **Lettre d’information au patient**
- **Questionnaire**
- **Guide de remplissage du questionnaire**

Lettre d'information adressée au patient

Centre de soins et de consultations dentaires
Service d'odontologie conservatrice et pédiatrique
CHU-HOTEL DIEU

Nantes, le 21 décembre 2001

Madame, Monsieur,

Vous avez reçu des soins au centre de consultations dentaires durant les années 1999, 2000 ou 2001.

Afin d'évaluer la qualité de nos traitements dans le cadre d'une **enquête épidémiologique**, nous réalisons un suivi après 1 ou 2 années

Nous vous proposons donc de venir au centre de soins dentaire pour un bilan bucco-dentaire.

Aucun honoraire ne vous sera demandé à cette occasion.

Pourriez-vous joindre notre secrétaire Madame Le Corre au **02.40.08.37.25** afin de fixer un rendez-vous à votre convenance pour cette consultation de suivi.

Avec nos remerciements anticipés.

Dr. B. ENKEL.

Programme Hospitalier de Recherche Clinique :
» Évaluation de l'endodontie au centre de soins dentaires »

Dr Bénédicte ENKEL - CSD de Nantes – Département d'odontologie conservatrice
Klervi COURTIEU – Faculté d'odontologie de Nantes – étudiante en 4eme année

Questionnaire 1

Le CSD de Nantes mène une étude de recherche scientifique : nous désirons évaluer les résultats à un an, des thérapeutiques endodontiques.
Nous proposons de réaliser une étude rétrospective sur l'évaluation de l'endodontie au CSD, en étudiant les dossiers de patients ayant subis un traitement endodontique, il y a un an minimum.

Cette étude sera menée en deux étapes successives. La première étape consiste à étudier le dossier « patient », à l'aide du questionnaire ci-dessous.
La deuxième étape est un entretien avec le patient, où sera proposé au patient, un second questionnaire sur sa situation sociale, un examen clinique et un examen radiographique.

N° ARC :

N° patient : Tel :

ne pas remplir le tableau

	Pas LOE	LOE
LW bonne		
LW nulle		

N° dent :

Vous devez remplir cette partie, de suite, sur le deuxième questionnaire.

N° ARC :

N° patient : Etiquette patient

Tel :

N° dent :

1-Quelles sont les dates de début et de fin de soin ? -début : ……
-fin : ……

2-Quel est le nombre de praticiens qui ont effectué le soin endodontique ?…….

3-Quel est le(s) niveau(x) du (des) praticien(s) qui a (ont) effectué le soin endodontique ?

D1

D2

D3

T1

Interne

Praticien hospitalier

4-Quel est le diagnostic de la dent causale ? vitale

nécrosée

LOE

élargissement ligamentaire

Reprise de traitement

5-Combien de canaux possèdent la dent traitée ? ……

6-Quelle est la complexité canalaire ? -normale

-courbure nombre de canaux intéressés :……

-calcifications nombre de canaux intéressés :……

7-Quel a été le champ opératoire mis en place ? -digue

-autres

-pas connaissance

8-Quel a été le nombre de séances nécessaires à l'obturation de la dent ?…..

9-Si l'obturation a été différée (nombre de séances supérieur à 1), quel(s) produit(s) a (ont) été utilisé(s) ?

-hydroxyde de calcium

-autres ……..

10-Quelle a été la technique utilisée pour la préparation canalaire ?

-manuellement assistée

-RC

11-Quelle a été la technique utilisée pour l'obturation ?

-condensation latérale

-gutta chaude

-mono cône scéllé

12-Sur la radiographie, quelle est la qualité de la longueur de travail :

-bonne

-sous-évaluée

-sur-évaluéé

13-Sur la radiographie, quelle est la qualité de la condensation ?

-bonne

-mauvaise

14-Sur la radiographie, quelle est la qualité de la longueur d'obturation :

-correspond à la longueur de travail

-ne correspond pas à la longueur de travail

-perte de longueur

-dépassement de matériau

-dégradation du matériau

15-Quelle est la date d'obturation coronaire ? ……..

16-Quel matériau a-t-il été utilisé pour l'obturation coronaire ? ……

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Klervi COURTIEU – Faculté d'odontologie de Nantes – étudiante en 4eme année

Questionnaire 2

Le CSD de Nantes mène une étude de recherche scientifique : nous désirons évaluer les résultats à un an des thérapeutiques endodontiques.
Nous vous proposons de répondre à des questions, de participer à un examen clinique et radiographique, au cours d'un entretien de 20 minutes avec un étudiant ou un praticien du CSD. Nous nous engageons à respecter la confidentialité de vos réponses.

L'entretien a-t-il été accepté ? -non cause : ……
-oui

Date de l'entretien : ……. Heure du rendez-vous : ……

N° ARC : ……

N° patient :……

N° dent :……

Nous vous proposons de répondre, dans un premier temps, à des questions concernant votre situation sociale et, dans un deuxième temps de procéder aux examens cliniques et radiographiques.

1-Quel âge avez-vous ? …… ans

2-Etes-vous né (e) en France ? -oui
-non Pays :……..

3-Etes-vous de nationalité française ? -oui
-non nationalité :……..

4-quel est votre niveau d'études ? (études menées à leur terme ou sanctionnées par un diplôme)

- jamais scolarisé
- primaire non achevé
- primaire (certificat d'études élémentaires)
- secondaire : premier cycle (BEPC, BEP ou CAP)
- secondaire : deuxième cycle (BAC)
- supérieur

5-Actuellement, exercez- vous un travail (une activité professionnelle)? -Oui

-Non

Si Oui · vous êtes : - salarié(e)

-non salarié

-autre

-(indépendant, à votre compte)

· vous travaillez à temps : - plein

-partiel

-autre

· vous êtes en : - CDI (contrat à durée indéterminée)

- CDD (contrat à durée déterminée)

- autre

Si Non · Quelle est votre situation ?

Vous êtes : - à la recherche d'un 1er emploi

- chômeur depuis moins de 6 mois

-chômeur depuis plus de 6 mois

- retraité ou en préretraite

- autre

préciser: ……..

6-Quelle est votre profession ou la dernière que vous ayez exercée (si actuellement vous êtes en inactivité) ?

Recueillir très précisément .....

Nous allons maintenant procéder à l'examen clinique.

7-Quel est l'état de la reconstitution coronaire de la dent traitée ?

-bon état
-infiltrée
-cassée
-partie

Nous allons finir l'entretien par une radiographie, à l'aide d'un anneau de Rhine. (la radio sera agrafée au questionnaire)

8-Quel est la santé péri apicale de la dent traitée ? -RAS
-élargissement ligamentaire
-lésion apicale

9-Comment est l'évolution ? -bonne □
-statu quo □
-cicatrisation □
-mauvaise □

10-Quelle est la décision thérapeutique à prendre ? -abstention
-retraitement
-extraction

Programme Hospitalier de Recherche Clinique :

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Klervi COURTIEU- UFR d'Odontologie de Nantes- Etudiante en 4eme année

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Guide de Remplissage du questionnaire

Chaque investigateur aura un numéro (n° ARC) a mettre en haut du questionnaire pour la traçabilité de l'information.
Mettre l'étiquette du patient et préciser son numéro de téléphone.
Si le patient n'a pas de numéro de téléphone, indiquer : NEANT.

Questions :

1.Les dates de début et de fin de soin concernent **un seul et même traitement endodontique.**

3 et 4:*« niveau des praticiens » et « diagnostic de la dent causale».*

Plusieurs cases peuvent être cochées à la fois.

6:*» courbure canalaire »*

Indiquer si les racines de la dent étudiée présentent une **courbure *moyenne*** pour ce type de dent.

Signaler la présence de coudure apicale ou de racine en baillonnette.

10:*» technique de préparation canalaire »*

RC pour rotation continue.

11:» *technique d'obturation »*

Les obturations à la gutta chaude englobent toutes les techniques d'obturation utilisant la gutta chauffée : condensation verticale à chaud, Microflow, Microseal, Mac Spadden, Ultrafile (injection de gutta percha chaude), Thermafile, Hérofile…

12:*» qualité de la longueur de travail »*

La longueur de travail semble-t-elle correcte à la radiographie **: à 0,5 à 1,5mm de l'apex radiographique.**

13:»*qualité de la condensation d'obturation »*

Apprécier uniquement à la radiographie si l'obturation est suffisamment radiodense.

14: »*qualité de la longueur d'obturation »*

Plusieurs items peuvent être cochés à la fois.

Ne pas oublier de spécifier si elle **correspond à la LW**, que cette LW soit bonne ou mauvaise initialement.

CASTELOT ENKEL Bénédicte : « Evaluation des thérapeutiques endodontiques ; intérêt éventuel d'un biomatériau ».

La thérapeutique endodontique est un acte difficile et la revue de la littérature montre que son taux de succès est incertain. Il est donc essentiel de comprendre quels sont les facteurs qui favorisent ou qui pénalisent le succès de la thérapeutique endodontique. Ce travail de recherche clinique a comme objectif l'identification de facteurs prédictifs des traitements réalisés au Centre de Soins Dentaires de Nantes et de savoir dans quelle mesure l'utilisation de matériaux bioactifs pourraient améliorer le pronostique de ces traitements. Ce travail se compose d'une première étude longitudinale rétrospective portant sur 185 sujets, suivie d'une étude longitudinale prospective sur 256 sujets. Une analyse de survie originale permet d'explorer la survie à long terme des traitements endodontiques mais surtout, de prédire le temps nécessaire à la cicatrisation périapicale, ce que peu d'études pronostiques avaient proposé jusqu'alors.
Comme les différents travaux publiés dans ce domaine, nos 2 cohortes ont mis en exergue l'importance de la pathologie initiale, ainsi que la qualité de préparation et d'obturation canalaire, associée à une restauration ou à une reconstitution corono-radiculaire précoce et définitive. Par rapport aux autres études, cette analyse montre que la survie des traitements continue à décliner après plusieurs années, que certains facteurs vont favoriser des échecs précoces, d'autres vont être responsables d'échecs tardifs. De plus, la cicatrisation périapicale est un processus qui requiert, dans la grande majorité des cas, plusieurs années pour s'achever totalement. De ces résultats sera ensuite discuté l'intérêt d'un biomatériau en endodontie.

Rubrique de classement : ODONTOLOGIE- ENDODONTIE

Mots clés français : Résultats thérapeutiques, traitement du canal radiculaire, analyse de survie, analyse multivariée, étude de cohorte, pronostic, cicatrisation, périodonte apical.

MeSH : Treatment outcome; root canal therapy, survival analysis, multivariate analysis, cohort study, prognosis, wound healing, periapical tissue.

Jury :

Professeur P. Farge	Rapporteur
Professeur F. Perez	Rapporteur
Professeur P. Weiss	Directeur
Professeur V. Rivain Sebille	Co-Directeur
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