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Periodontal Regenerative Therapy in Endo-Periodontal Lesions: a case report

Universidade Fernando Pessoa

Faculdade Ciências da Saúde

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"Work presented to Fernando Pessoa University as

part of the requirements to achieve the

Master's Degree in Dentistry."

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(Cláudia Isabel Pires Ferreira da Silva)

Abstract

Endo-Periodontal Lesions can be defined as lesions in the periodontal and pulpar tissues of the same tooth, either in isolation or combined. Its prognosis may vary from favorable to hopeless and, according to prognostic classification systems, any hopeless tooth should be extracted. A growing body of evidence has suggesting otherwise. The aim of this thesis is to report a clinical case with a 3-year follow-up assessing the outcome of endodontic and periodontal treatment of a hopeless tooth and, with this, present and discuss new horizons and solutions for Endo-Periodontal Lesions beyond the apex. It is concluded that Periodontal Regenerative Therapy can be an effective conservative treatment for teeth with a hopeless prognosis and, therefore, should be considered by clinicians as a valid intervention.

Keywords: “Periodontal Regenerative Therapy”; “Endo-periodontal lesions”; “Endodontic therapy”; “Prognosis”; “Hopeless tooth”.

Resumo

As Lesões Endo-Periodontais podem ser definidas como uma lesão nos tecidos periodontal e pulpar de um determinado dente, de forma isolada ou combinada. O seu prognóstico pode variar de favorável a *hopeless*, sendo que, segundo os sistemas de classificação de prognóstico, qualquer dente *hopeless* deve ser extraído. Um crescente corpo de evidência científica tem demonstrado o contrário. O objetivo deste trabalho é descrever um caso clínico com 3 anos de *follow-up* avaliando o resultado do tratamento endodôntico e periodontal de um dente *hopeless* e, com isso, mostrar e discutir novos horizontes e soluções para as Lesões Endo-Periodontais para além do ápice. Conclui-se que, para lidar com Lesões Endo-Periodontais em dentes com prognóstico *hopeless*, tratamentos conservadores, como a Terapia Periodontal Regenerativa, devem ser considerados pelos clínicos como uma opção válida.

Palavras-chave: “Terapia Periodontal Regenerativa”; “Lesões Endo-periodontais”; “Terapia Endodôntica”; “Prognóstico”; “Dente sem esperança”.

Dedicatory

À minha família:

Tudo aquilo que sou, devo-o a vocês.

Ao meu namorado:

Esta conquista, devo-a a ti.

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Abbreviation Index

CNRCT: Conventional Non-Surgical Root Canal Treatment

EMD: Enamel matrix derivates

EPL: Endo-Periodontal Lesions

EPR: Extraction and Prosthetic Replacement

PPD: Probing pocket depth

PRT: Periodontal Regenerative Therapy

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1 – Introduction

Periodontal and endodontic tissues are connected, not only in an anatomical and functional sense, but also from a common embryological origin (Peeran et al., 2013). These connections allow for endodontic and periodontal lesions to coexist and influence each other. This finding was first reported by Turner and Drew (1919) and Henrichi and Hartzell (1919), although its clinical relevance remained unexplored until the pioneer work of Simring and Golberg (1964).

Presently, the evaluation (Rotstein, 2017), diagnosis and treatment procedures (Peeran et al., 2013; Rotsein, 2017), and prognosis accuracy (Rotstein, 2017) for Endo-Periodontal Lesions (EPL) call for improvement. Its low prevalence (Herrera et al., 2018) makes it difficult to investigate and, therefore, to improve the aforementioned tools.

1.1 – Endo-Periodontal Lesions

An EPL can be defined as a lesion in the periodontal and pulpar tissues of the same tooth, either in isolation or combined (Papapanou et al., 2018). This condition might be caused by microorganisms as well as contributing factors, i.e. poor endodontic treatment, poor restoration, trauma, root resorptions, perforations, fractures and dental malformations (Rotstein, 2017). Once the infection takes place, it can spread into the dental pulp and periodontal ligament through anatomical (i.e. apical foramen, lateral or accessory root canals and dentine tubules) (Zehnder et al., 2002; Rotstein, 2017; Ricucci et al., 2021) and non-anatomical (i.e. iatrogenic root canal perforations, vertical root fracture) factors (Zehnder et al., 2002). This communication between tissues is one of the factors that most contributes to the difficulties faced when addressing this condition (Papapanou et al., 2018).

According to Ricucci et al. (2021), severe pulp reactions can be seen in periodontal lesions to and beyond the apex, because of spreading through the aforementioned pathways. As a consequence of spreading, bone destruction may occur. In case of an infection of periodontal origin, bone destruction may occur in the coronal-apical direction, whereas an infection of endodontic origin will cause bone destruction in an opposite direction (Rotstein, 2017).

Based on the possible aetiologies of EPL, a classification was proposed by Rotstein and Simon (2004), who tried to enlighten the way in which diagnosis, treatment and prognosis could be carried out more effectively. Through this classification, EPL can be defined as (1) primary

endodontic disease; (2) primary periodontal disease, or; (3) combined lesions. The latter can be subdivided in primary endodontic lesions with secondary periodontal involvement, primary periodontal lesions with secondary endodontic involvement and true combined disease.

1.2 – Differential diagnosis

In order to treat these lesions appropriately, it's important to understand the cause of the condition (Bergenholtz et al., 2015; Rotstein, 2017; Herrera et al., 2018). These lesions may be diagnosed as arising from an endodontic or periodontal cause, as well as from both. Understanding the cause requires pulpar vitality testing, history taking (e.g. occurrence of trauma), evaluating the general condition of the tooth and periodontium, the presence of cavities and large and deep restorations. The findings of the objective examination should be confirmed with the use of complementary diagnostic exams, e.g., peri-apical radiography (Bergenholtz et al., 2015; Rotstein, 2017; Herrera et al., 2018).

From the above, the main test is the pulpar vitality evaluation, although the chance of false positives or false negatives (Bergenholtz et al., 2015). To reduce these possibilities, different testing methods should be employed and analysed, for a more accurate diagnosis.

The diagnosis may vary according to the findings (Bergenholtzet al., 2015): (1) if the tooth is vital, the cause is periodontal and the treatment should be in accordance; (2) if the tooth is not vital, the cause may be endodontic or endo-periodontal, requiring endodontic treatment as first line. In the latter cases, if the lesion responds positively to endodontic treatment, the endodontic cause is confirmed (Bergenholtzet al., 2015). If, however, there is not improvement with endodontic treatment, the cause may be assumed to be endo-periodontal and further periodontal therapy should be started.

1.3 – Hopeless teeth

According to McGuire and Nunn (1996) a tooth could be classified as hopeless when presenting inadequate osseous insertion to the point of inability to "maintain health, comfort and function". Kwok and Caton (2007) improved on McGuire and Nunn's classification by introducing a prognostic system which accounted for periodontal stability and on the evaluation of evidence-based general modification factors (i.e. patient compliance, smoking habits, diabetes mellitus

and other systemic conditions) and local modification factors (i.e. deep probing depth and attachment loss, anatomic plaque-retentive factors, occlusion or parafunctional habit related traumas, tooth mobility). Based on this classification, any hopeless tooth should be extracted, as it would imply an unrepairable destruction of dental support tissue (Kwok and Caton, 2007).

The prognosis for a tooth with EPL may vary from favourable to hopeless (Herrera et al., 2018). The distinction between the different prognosis can be made considering the cause, extension of periodontal destruction around the affected tooth, and the presence and severity of the periodontal disease affecting the patient's oral health.

In the beginning of the Modern Periodontology era, it was shown that in teeth with severe periodontal support loss, there was a chance of avoiding extraction if the teeth were kept healthy within a strict periodontal therapy and periodontal care program (Lindhe and Nyman; 1984; Axelsson et al., 2004; Pretzl et al., 2009a; Chambrone et al., 2010; Bäumer, et al. 2011; Ng et al., 2011; Cortellini.and Tonetti, 2015). Additionally, periodontal regeneration has shown the potential to allow long-term tooth preservation whenever teeth present deep pockets associated with intra-bony defects (Cortellini and Tonetti, 2004; Sculean et al., 2008; Huynh-Ba et al., 2009; Pretzl et al., 2009b; Nygaard-Østby et al., 2010; Cortellini and Tonetti, 2015). The development of endodontic and periodontal materials and techniques brought new light to the matter improving the prognosis and intervention in EPL in favour of more conservative treatment plans in spite of current guidelines (Sanz et al., 2020) not providing any information regarding hopeless teeth, as there are still thought of as cases for extraction (McGuire and Nunn, 1996; Kwok and Caton, 2007).

1.4 – Treatment

Periodontal Regenerative Therapy (PRT) is a histological concept of surgical treatment in which there is a reconstruction of periodontal support tissues (i.e., cementum, periodontal ligament and alveolar bone) destroyed by periodontal disease (Rios et al., 2015). The surgical procedures employed are complemented with the isolated or combined application of materials (i.e., bone grafts and bone substitutes, guided tissue regeneration, enamel matrix derivate (EMD) and growth and differentiation factors) (Sculean, 2017). The material selection follows the rationale proposed by Sculean (2017).

The success of this intervention relies on patient-, tooth- and defect-based factors and can be clinically confirmed through observation of a reduction in probing depth, increased clinical attachment level and radiographic imaging compatible with osseous filling (Cortellini and Tonetti, 2015; Rios et al., 2015).

Cortellini et al. (2011) and Cortellini et al. (2020), a 5-year follow-up and 10-year follow-up of the same sample, respectively, present some of the most important reports on PRT efficacy by reporting an 88% success rate in reversing hopeless tooth prognosis to a favourable one over a 10-year period. The improvements were reported within measures of stability, function and comfort in an experimental group of 25 teeth with periodontal lesions to and beyond the apex. In these studies, the surgical procedure for those teeth with periodontal lesion beyond the apex included a Conventional Non-Surgical Root Canal Treatment (CNRCT) which preceded the instrumentation of the root apex, as it required cutting of the neurovascular supply to the tooth (Cortellini et al., 2020).

Cortellini et al. (2011) defined the following inclusion criteria for the application of PRT: (1) good general health; (2) smoking status < 20 cigarettes/day; (3) good oral hygiene: full mouth plaque score ≤ 25%; (4) low levels of residual infection: full mouth bleeding score ≤ 25%; (5) optimal compliance; (6) presence of severe generalized periodontal disease (attachment loss ≥ 6mm at ≥ 30% of sites); (7) presence of at least one tooth to be extracted for periodontal reasons; and (8) endodontic status: both vital and non-vital teeth were included.

The experimental group received PRT 3 months after CNRCT. The procedure entailed a papilla preservation flap and the application of regenerative material, i.e. EMD, non-resorbable and bio-resorbable barrier membranes and bone substitute (Cortellini et al., 2011). This group received the following techniques (Cortellini et al., 2011): (1) exclusively EMD in 10 patients; (2) exclusively barrier membranes in 4 patients, from which, 2 were non-resorbable titanium-reinforced barriers and 2 were bio-resorbable; (3) combination of bio-resorbable barrier membrane and bone substitute in 4 patients; (4) combination of EMD and bone substitute in 5 patients, and; (5) combination of EMD and bio-resorbable barrier membrane in 2 patients.

This intervention has been proven to provide favourable results throughout the years as several researchers (Agrali and Kuru, 2015; Pico-Blanco et al., 2016; Fahmy et al., 2016; Alquthami et al., 2018; Carranza and Rojas, 2018; Oh et al., 2019, Katwal et al., 2020; Grigorie et al., 2021) have reproduced the results of Cortellini et al. (2011). This growing body of evidence has been

strengthening the role of PRT in conjunction with CNRCT as a viable alternative for teeth with a hopeless prognosis.

1.5 –Extraction and Prosthetic Replacement versus Periodontal Regenerative Therapy

Extraction and Prosthetic Replacement (EPR) is a highly successful option for EPL (Cortellini et al., 2020). However, when compared to PRT the total cost for EPR is substantially higher than that of PRT. Besides being costlier and despite having good success rates, EPR also has an increased risk of further interventions (Wennström and Lang, 2015; Matarasso et al., 2010; Roccuzzo et al., 2010) due to these patients having a higher risk of peri-implantitis (Mengel et al., 2017; Anderson et al., 2020) and mucositis, lower rates of implant success and survival (Mengel et al., 2017; Berglundh et al., 2015), higher marginal bone loss and increased inflammation in peri-implant soft tissues (Berglundh et al., 2015), unlike those who enrol PRT. PRT also showed high success rates for up to 10 years in hopeless teeth (Cortellini et al., 2020), and up to 20 years in other periodontal conditions (Cortellini et al., 2017). Pico-Blanco et al. (2016) reported a clinical case with 17 years follow-up, in which a hopeless tooth was successfully treated with a combination of endodontic therapy and PRT. Pini Prato and Cortellini (2016) reported a clinical case with 30 years follow-up, in which a deep intrabony defect was successfully treated with a combination of PRT and mucogingival surgery. Considering the literature supporting the use of PRT (Agrali and Kuro, 2015; Pico-Blanco et al., 2016; Fahmy et al., 2016; Alquthami et al., 2018; Carranza and Rojas, 2018; Oh et al., 2019; Katwal et al., 2020; Grigorie et al.,2021) its economic benefits (Cortellini et al., 2020) and lower risks when compared to EPR, PRT should be the main option for hopeless teeth.

The interest of this therapy relies on its ability to delay the application of implants. This is particularly important in younger patients, as hopeless teeth can be found in individuals still in their late 20’s, like in Alquthami et al. (2018) case report, i.e. a 27-year-old female.

The aim of this article is to report a clinical case with a 3-year follow-up assessing the outcome of endodontic and periodontal treatment of a hopeless tooth and, with this, present and discuss new horizons and solutions for EPL beyond the apex.

1.6 – Materials and Methods

In order to assemble the clinical case and collect the patient's data, authorisation was requested from the Ethics Committee of Fernando Pessoa University, whose assent was given on May 14th, 2021 (Attachment III), followed by an authorisation request from the Directorate of Pedagogical Clinics in Dentistry, at the Health Sciences Faculty of the Fernando Pessoa University, whose approval on May 28th, 2021. The data was collected between the months of May 2021 and June 2021 during some appointments within the Curricular Unit of "Periodontia III", in the Pedagogical Clinics of Dentistry, at the Health Sciences Faculty of Fernando Pessoa University. The author participated in clinical care as an assistant, guided by the professors responsible for supervising and guiding the present work. The follow-up was carried out on March 23rd, 2021, in which an Informed Consent was signed (Attachment IV) by the patient, allowing the authors to use his data, photographs, images and disclosure of the case for study purposes, under the condition of full anonymity.

Online databases (PubMed, B-On and Web of Science) and specialty books were consulted for the writing of the literature review in the introduction section. The retrieval of literature was conducted according to the following inclusion criteria: (1) articles published between 1900 and 2021; (2) consideration for the design of the study (Clinical Practice Guidelines; Meta-Analysis; Systematic Review; Randomised Controlled Trial; Cohort and Cross-Sectional Observational Studies, and; Narrative Review); (3) reference works in the fields of periodontal regenerative therapy and endo-periodontal lesions, and; (4) references listed in the articles selected. The exclusion criteria considered were: (1) studies that did not used periodontal regenerative therapy; (2) studies without a clear methodology, and; (3) studies with a design whose strength of evidence was below that of those mentioned above. In the search process the following keyword were used, separated by the Boolean operator "AND": "Periodontal Regenerative Therapy"; "Endo-periodontal lesions"; "Endodontic therapy"; "Prognosis"; "Hopeless tooth". From the results obtained, 153 articles were selected by title, 62 by abstract and 46 were select after reading the full text.

2 – Clinical Case

On 15th of March 2018, a 68-year-old man attended to the Pedagogical Clinics of Dentistry, at the Health Sciences Faculty of Fernando Pessoa University with complaints of frequent abscesses in the maxillary left canine (tooth #23).

Upon medical history taking, the patient reported to be diagnosed with Type II Diabetes Mellitus. He referred non-smoking habits.

The periodontal and radiographic (panoramic + periapical radiography) evaluation showed a total loss of insertion in the vestibular area of the tooth #23. The probing pocket depth (PPD) was 6 mm in mesio-buccal and greater than 12 mm in buccal (Figure 1) and disto-buccal regions, with bleeding on probing. There was grade III tooth mobility for this tooth and the thermal sensitivity cold test showed to be positive. The adjacent teeth revealed no increased PPD (Attachment 1 - Initial Periodontogram). Afterwards the process of examining the case, it was possible to diagnose an EPL with primary periodontal disease.

Figure 1 – Probing pocket depth in buccal.
(The recording of this image took place right before the surgery)

This evaluation allowed to classify the tooth #23 as having a hopeless prognosis according to Kwok and Caton (2007).

After Non-Surgical Periodontal Treatment and discussing possible therapies with the patient, it was decided to perform the CNRCT in a first phase, followed by PRT and a supportive periodontal care program. Although the tooth was vital, endodontic treatment was performed as the bony defect was present beyond the apex. At the end of the appointment, the patient was given instructions and motivation regarding oral hygiene, revised and reinforced at every appointment.

On the 2nd and 3rd of May 2018, the endodontic treatment was performed, with the application of calcium hydroxide medication between appointments.

One month after CNRCT, the patient presented, once more, complaints due to abscesses in tooth #23.

The second phase of the treatment plan, which consisted on a surgical procedure, was executed after a 6-month follow-up period, on 30th of November 2018. (Figure 2)

Figure 2 – Periapical radiography after a 6-month follow-up.

Once the tooth presented hypermobility, it was splinted to the adjacent teeth before surgery.

Local anaesthesia (6 x 1.8mL of 2% articaine hydrochloride with 1:100,000 epinephrine) was administered. A papilla preservation flap was raised, and a releasing incision was performed distally to the upper left pre-molar tooth (#24). After removing the inflamed tissue and calculus from the root surface with ultrasonic tips (Figure 3 and Figure 4) and applying EDTA (Straumnn AG) as indicated by the manufacturer, EMD (Straumann AG, Basel, Switzerland) and bone substitute (Bio-Oss, Geistlich, Wolhusen, Switzerland) were placed into the bony defect (Figure 5).

Figure 3 – Photograph before removing the inflammation tissue and calculus.

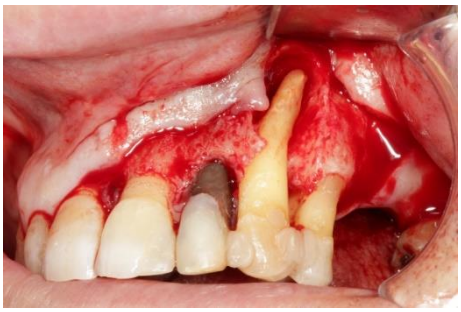


Figure 4 – Photograph after removing the inflammation tissue and calculus.

Figure 5 – Bone defect filled with EMD and bone substitute.

After, a resorbable barrier membrane (Bio-Gide, Geistlich, Wolhusen, Switzerland) was placed above the bone graft (Figure 6). The flap was then repositioned and sutured with 5-0 Polypropylene thread (Figure 7).

Figure 6 – Resorbable membrane positioning.

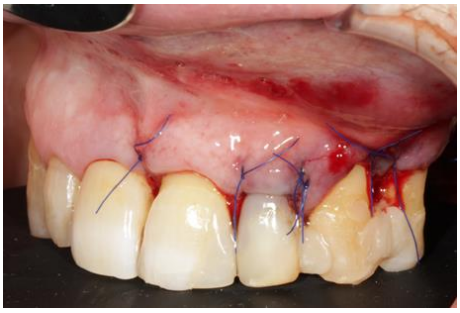


Figure 7 – Primary wound closure, immediately after the surgery.

After surgery, post-operative recommendations were given and Amoxicillin (875 mg) + Clavulanic Acid (125 mg), Paracetamol (1 g), Ibuprofen (600 mg) (8 days) and mouth rinses with Chlorhexidine 0,12% (3 times/day, 1 month) were prescribed. The patient was cautioned against brushing, flossing and chewing on the area of the procedure for a period of 3 to 8 weeks, after which, the instructions and motivation given in the first appointment were reintroduced.

During the month of December 2018, there were 3 post-operative evaluation consultations, and in the last one, on December 19, the suture was removed. There were no postoperative complications.

During the 5 months that followed, from January to May 2019, monthly consultations were performed, with oral hygiene instructions and reinforcement. In March 2019, 4 months after the surgical intervention, a periapical radiography was taken (Figure 8). The splint was then removed later that same year, in May.

Figure 8 – Periapical radiography 4 months after the surgical intervention.

In 2020, 3 consultations were carried out (February, June and September). In the last appointment the tooth #23 was classified as having a questionable prognosis, according to

Kwok and Caton (2007). The patient confessed not to perform adequate oral hygiene. The patient was, once again, instructed and motivated for oral hygiene.

In a new appointment, on 23rd March 2021, after several follow-ups over 3 years, the periodontal and radiographic evaluation showed stable parameters (Figure 9 and Figure 10). Upon medical history taking, the patient informed to have been recently diagnosed with Rheumatoid Arthritis.

Figure 9 – 3-years follow-up photography.

Figure 10 – 3-years follow-up periapical radiography.

The results of the periodontal evaluation showed a PPD of 3 mm in mesio-buccal, 5 mm in buccal and 2 mm in disto-buccal regions (Attachment 2 – Re-evaluation Periodontogram) and the results of the clinical and radiographic examinations showed radiographic bone-filling with an increase in clinical attachment of the tooth. It presents physiological mobility, compatible with the preservation of the tooth in function, comfort and health in the oral cavity. This evaluation allowed to classify this tooth as having a favourable prognosis according to the classification proposed by Kwok and Caton (2007).

3 – Discussion

In this case report it was possible to improve the prognosis of a hopeless tooth. In order to do so, a tooth with primary periodontal lesion and attachment loss beyond the apex received a combined treatment of CNRCT and PRT. The result showed the tooth progress to a favourable prognosis, as defined by Kwok and Caton (2007), at the time of the 3-year follow-up.

This patient presented a primary periodontal lesion that extended beyond the apex. Although the tooth was vital, the nature of the lesion required an instrumentation process in which the neurovascular supply to the tooth had to be cut. In anticipation, a CNRCT was performed. Besides allowing for a complication-free cut of the neurovascular bundle, this procedure was also beneficial as periodontal lesions to and beyond the apex result in consequential severe pulp reactions (Ricucci et al., 2021). PRT was followed, according to the protocol described by Cortellini et al. (2011). However, there were 2 exceptions to the protocol: (1) instead of a 3 month waiting period between the CNRCT and PRT, the procedures were performed 6 months apart, due to the closing of the clinic at the end of the school year in which the treatments began, and; (2) the inclusion of EMD with the combination of bio-resorbable barrier and bone substitute described in the article. The decision to add EMD was two-fold: on the one hand, the material was destined for a surgery that did not take place, which lead to repurposing the application of EMD to this patient, free of charge; and on the other hand, due to the extent of the lesion, the application of EMD had the intent to optimize the periodontal regeneration. This inclusion of EMD is in line with the rationale for PRT proposed by Sculean (2017).

Regarding the combination of materials, from the 5 options presented by Cortellini et al. (2011) the aforementioned option was chosen considering the depth and width of the periodontal defect.

There was a shortcoming in the regeneration process, proven by the reminiscing pocket in buccal, although its origin cannot be ascertained for sure. Patient collaboration is one of the most relevant modifiable factors for the success of this procedure (Lindhe and Nyman; 1984; Axelsson et al., 2004; Kwok and Caton, 2007; Pretzl et al., 2009a; Chambrone et al., 2010; Bäumer, et al. 2011; Ng et al., 2011; Cortellini.and Tonetti, 2015); therefore, the lack of it – as confessed by the patient in September 2020 – could have influenced the outcome of the regeneration process. The impact of compliance with recommendation can also be seen through the improvement from a questionable prognosis to a favourable one in six months, after the patient improved his oral hygiene. However, PRT might have been unable to lead to a full

regeneration even with the patient's full compliance, as it has a regeneration efficacy, not only in hopeless teeth but in other conditions, of 68%-100% (Cortellini and Tonetti, 2004; Huynh-Ba et al., 2009; Pretzl et al., 2009b; Cortellini et al., 2011; Cortellini et al., 2017; Oh et al., 2019; Cortellini et al., 2020).

In this case report, it was necessary to perform a CNRCT procedure because, in the process of clearing the infected periodontal area during instrumentalization in the PRT procedure, the neurovascular bundle could not be preserved. Therefore, further endodontic complications were prevented with the CNRCT. As the lesion extended beyond the apex, the protocol was easy to define, unlike periodontal lesions that only extend to the root apex.

With this in mind, one could question what would be the right approach in vital teeth with periodontal lesions to the apex, since there is histological evidence of severe pulp reactions, although it cannot be clinically proven and current clinical decision-making does not take into consideration the findings of Ricucci et al. (2021), yet. Another question could be posed, regarding the role of endodontic treatment in teeth with periodontal lesion to the apex: could the application of endodontic treatment in these teeth result in better outcomes? These questions are born out of conflicting histological and clinical evidence on the development of pulpar infection secondary to periodontal disease to or beyond the apex, since Ricucci et al. (2021) reports that the presence of periodontal lesion to or beyond the apex would lead to severe pulp reactions, whereas in Cortellini et al. (2011) only 1 vital tooth out of 4 with periodontal lesion to the apex that benefited from PRT suffered necrosis, implying that loss of vitality is not a guaranteed consequence of periodontal lesion to or beyond the apex. This reality creates a conundrum regarding the clinical use of the information reported by Ricucci et al. (2021) while also prompting the question of how to detect in which teeth the asymptomatic pulp reactions secondary to periodontal lesions to the apex may or may not lead to symptomatic pulp infections. Answering this question could bridge histological and clinical evidence to provide more accurate prognostic tools for EPL.

Economy-wise, PRT seems to be a better option for EPL, especially when compared to the alternative – EPR. Cortellini et al. (2020) compared the cost of both interventions over a 10-year period reporting substantially lower costs with PRT. In their study, Cortellini et al. (2020) showed that PRT was less costly than EPR, overall, even when added 3 extractions in the PRT group. Moreover, EPR brings several risks of future complications and interventions

(Matarasso et al., 2010; Rocuzzo et al., 2010; Berglundh et al., 2015; Wennström and Lang, 2015; Mengel et al., 2017; Anderson et al., 2020) that are not seen with PRT.

Hopeless teeth have been reported in patients in their 20's (Alquthami et al., 2018). If extraction is performed and no complications arise, young patients will very likely still have to endure further procedures and, being EPR an end-of-line treatment, more conservative and cheaper options available should be considered. As part of the role of the dentist, as a healthcare professional, is to ensure that the patient is provided with all the supported and available options with the present and future in mind, dentists should be mindful of how quickly last resort options might be being provided to patients who could avoid or delay them, over more plausible options such as PRT. Therefore, PRT seems to be a better option for extraction for younger population and should be proposed to patients as a better long-term option over extraction, whenever possible.

All and all, this case report not only shows a successful case of PRT in a hopeless tooth, but also calls for the lack of recognition it has been given as a viable, economically sound and safer option for hopeless tooth, when compared to extraction. This lack of recognition for PRT is evident in current guidelines (Sanz et al., 2020) and prognostic systems (Kwok and Caton, 2007), as the former fails to provide orientation for managing periodontal disease past stage 4 and the latter associates hopeless teeth with an irreversible prognosis of extraction, despite evidence of the contrary, as this study and others before it (Cortellini et al., 2011; Agrali and Kuro, 2015; Pico-Blanco et al., 2016; Fahmy et al., 2016; Alquthami et al., 2018; Carranza and Rojas, 2018; Oh et al., 2019; Katwal et al., 2020; Cortellini et al., 2020; Grigorie et al.,2021). If guidelines were to be produced to include PRT as an option for hopeless teeth, orientations should be given for correct patient selection, following the recommendations of Cortellini et al. (2011). Moreover, the update of prognostic systems is a must as, currently, the evidence backing those systems can be considered outdated. The lack of consideration for PRT in cases of hopeless teeth disables clinicians from providing their patients with all the available information and options of care. Although some works (Cortellini et al., 2020; Pico-Blanco et al., 2016) report evidence of up to 10 and 17 years, respectively, of effectiveness of PRT for hopeless teeth, if longer studies where to be conducted, this time frame could possibly be improved, as one trial as already shown effectiveness of PRT in a 20-year follow-up in patients with intrabony defects (Cortellini et al., 2017) and a case report of a deep intrabony defect treated with a combination of PRT and mucogingival surgery has shown efficacy in a 30-year follow-up (Pini Prato and Cortellini, 2016).

This case report presents some limitations, most of which relate to imaging and photographic report. It was not possible to retrieve the initial periapical radiographic imaging, disabling us to present the complete documentation of the case, despite it not being relevant for the present study as Figure 2 shows the patient before surgery as there were no aggravation of the condition since the patients' admission. The photography showing progress at 3-year follow-up failed to show the PPD which limits the demonstration of the correction of the intraosseous defect, although this was merely for demonstrative effects as the study presents the radiographic imaging and clinical documentation validating the improvement of the condition. Considering the recommendations in Cortellini et al. (2011) about the ideal patient subpopulation for PRT, the patient did not fit this subpopulation, due to non-compliance, which hindered the regeneration process, although not the procedure's success. Appropriate patient selection could prevent these setbacks. Besides what has been stated, another possible limitation is the lack of existing evidence on the subject. Cortellini et al. (2020) is the only piece of evidence reporting a long-term follow-up on the efficacy of PRT in hopeless teeth. All other studies are case reports, case series or clinical trials, with no reviews produced to date. More evidence would clarify the role of PRT on hopeless teeth and provide further theoretical and clinical information on its application.

This case report contributes to the existing body of literature informing on the role of PRT in hopeless teeth. This study has been able to show a case of a reversion of a hopeless prognosis to a favourable one in a 68-year-old patient with periodontal lesion beyond the apex during a 3-year period. This not only shows the potential of PRT as a first-line approach for hopeless teeth but also calls for the inclusion of PRT as a treatment for hopeless teeth in periodontal care guidelines. Prognostic systems ought to be revised to contemplate on the information about the reversibility of a hopeless prognostic. Further studies should be conducted in the form of clinical trials with a variety of presentations of hopeless teeth over considered periods of time to ensure that the effect of PRT in these cases can be well established and consistently reproduced.

4 – Conclusions

This case report shows a successful case of periodontal lesion beyond the apex with a hopeless prognosis reverted to a favourable prognosis in an upper left canine tooth of a 68-year-old patient, 3 years after its treatment with PRT. The importance of appropriate patient compliance with recommendations is shown, specifically how the lack of it may compromise a sound and effective clinical approach. It also refers to the importance of knowing if the patient belongs to the most appropriate subpopulation for the performance of PRT on a hopeless tooth. This article shows the possibility for reversion of a hopeless prognosis and can help motivate a call for revision of guidelines with regards to current prognostic systems and recommended treatments. To deal with EPL with a hopeless prognosis, conservative treatments, such as PRT, should be considered, by clinicians, as a first-line intervention instead of an end-of-line treatment, as happens in current practice. This change in perspective could lead to lower costs and risk of future interventions. In conclusion, this case report serves as evidence that there can be hope for hopeless teeth.

5 – Bibliography

Agrali, O. and Kuru, B. (2015). Periodontal treatment in a generalized severe chronic periodontitis patient: A case report with 7-year follow-up. *European Journal of Dentistry*, 9(2), pp. 288–292.

Alquthami, H. et al. (2018). Successful management of teeth with different types of endodontic-periodontal lesions, *Case Reports in Dentistry*, 2018(1), pp. 1–8.

Anderson, N. et al. (2020). Retrospective Analysis of the Risk Factors of Peri-implantitis. *The Journal of Contemporary Dental Practice*, 21(12), pp. 1350–1353.

Axelsson, P., Nyström, B. and Lindhe, J. (2004). The long-term effect of a plaque control program on tooth mortality, caries and periodontal disease in adults. Results after 30 years of maintenance. *Journal of Clinical Periodontology*, 31(9), pp. 749–757.

Bäumer, A. et al. (2011). Patient-related risk factors for tooth loss in aggressive periodontitis after active periodontal therapy. *Journal of Clinical Periodontology*, 38(4), pp. 347–354.

Bergenholtz, G. et al. (2015). Endodontics and Periodontics. *In:* Lang, N. and Lindhe, J. (Ed). *Clinical Periodontology and Implant Dentistry*. 6th ed. Chichester. Wiley Blackwell, pp. 830–860.

Berglundh, T., Lindhe, J. and Lang, N. (2015). Peri-implant Mucositis and Peri-implantitis. *In:* Lang, N. and Lindhe, J. (Ed). *Clinical Periodontology and Implant Dentistry*. 6th ed. Chichester. Wiley Blackwell, pp. 505–517.

Carranza, N. and Rojas, M. (2019). Treatment of an Advanced Gingival Recession Involving the Apex of the Tooth: Periodontal Plastic, Endodontic Surgical Approach With a Laterally Stretched Flap and a Connective Tissue Graft. *Clinical Advances in Periodontics*, 9(2), pp. 70–76.

Chambrone, L. et al. (2010). Predictors of tooth loss during long-term periodontal maintenance: a systematic review of observational studies. *Journal of Clinical Periodontology*, 37(7), pp. 675–684.

Cortellini, P. and Tonetti, M. (2004). Long-term tooth survival following regenerative treatment of intrabony defects. *Journal of Periodontology*, 75(5), pp. 672–678.

Cortellini, P. et al. (2011). Periodontal regeneration versus extraction and prosthetic replacement of teeth severely compromised by attachment loss to the apex: 5-year results of an ongoing randomized clinical trial. *Journal of Clinical Periodontology*, 38(10), pp. 915–924.

Cortellini, P.and Tonetti, M. (2015). Clinical concepts for regenerative therapy in intrabony defects. *Periodontology 2000*, 68(1), pp. 282–307.

Cortellini, P. et al. (2017). Periodontal regeneration compared with access flap surgery in human intra-bony defects 20-year follow-up of a randomized clinical trial: tooth retention, periodontitis recurrence and costs. *Journal of Clinical Periodontology*, 44(1), pp. 58–66.

Cortellini, P. et al. (2020). Periodontal regeneration versus extraction and dental implant or prosthetic replacement of teeth severely compromised by attachment loss to the apex: A randomized controlled clinical trial reporting 10-year outcomes, survival analysis and mean cumulative. *Journal of Clinical Periodontology*, 47(6), pp. 768–776.

Fahmy, M. et al. (2016). Treatment of a Periodontic-Endodontic Lesion in a Patient with Aggressive Periodontitis. *Case Reports in Dentistry*, 2016.

Grigorie, M. et al. (2021). Hopeless tooth? Prognosis and comprehensive treatment. A case report. *Journal of Medicine and Life*, 14(2), pp. 287–294.

Henrici, A. and Hartzell, T. (1919). The Bacteriology of Vital Pulps. *Journal of Dental Research*, 1(4), pp. 419–422.

Herrera, D. et al. (2018). Acute periodontal lesions (periodontal abscesses and necrotizing periodontal diseases) and endo-periodontal lesions. *Journal of Clinical Periodontology*, 45(Suppl 20), S78–S94.

Huynh-Ba, G. et al. (2009). The effect of periodontal therapy on the survival rate and incidence of complications of multirooted teeth with furcation involvement after an observation period of at least 5 years: a systematic review. *Journal of Clinical Periodontology*, 36(2), pp. 164–176.

Katwal, D. et al. (2020). Successful Multidisciplinary Management of an Endodontic-Periodontal Lesion Associated With a Palato-Radicular Groove: A Case Report. *Clinical Advances in Periodontics*, 10(2), pp. 88–93.

Kwok, V. and Caton, J. (2007). Commentary: prognosis revisited: a system for assigning periodontal prognosis. *Journal of Periodontology*, 78(11), pp. 2063–2071.

Lindhe, J. and Nyman, S. (1984) Long-term maintenance of patients treated for advanced periodontal disease. *Journal of Clinical Periodontology*, 11(8), pp. 504–514.

Matarasso, S. et al. (2010). A 10-year retrospective analysis of radiographic bone-level changes of implants supporting single-unit crowns in periodontally compromised vs. periodontally healthy patients. *Clinical Oral Implants Research*, 21(9), pp. 898–903.

McGuire, M. and Nunn, M. (1996). Prognosis Versus Actual Outcome. II. The Effectiveness of Clinical Parameters in Developing an Accurate Prognosis. *Journal of Periodontology*, 67(7), pp. 658–665.

Mengel, R., Heim, T. and Thöne-Mühling, M. (2017). Mucositis, peri-implantitis, and survival and success rates of oxide-coated implants in patients treated for periodontitis 3-to 6-year results of a case-series study. *International Journal of Implant Dentistry*, 3(1), p. 48.

Ng, M. et al. (2011). Tooth loss in compliant and non-compliant periodontally treated patients: 7 years after active periodontal therapy. *Journal of Clinical Periodontology*, 38(5), pp. 499–508.

Nygaard-Østby, P. et al. (2010). Periodontal healing following reconstructive surgery: effect of guided tissue regeneration using a bioresorbable barrier device when combined with autogenous bone grafting. A randomized-controlled trial 10-year follow-up. *Journal of Clinical Periodontology*, 37(4), pp. 366–373.

Oh, S., Chung, S. and Han, J. (2019). Periodontal regenerative therapy in endo-periodontal lesions: A retrospective study over 5 years. *Journal of Periodontal and Implant Science*, 49(2), pp. 90–104.

Papapanou, P. et al. (2018). Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Periodontology*, 89(Suppl 1), S173–S182.

Peeran, S. et al. (2013). Endo-Perio Lesions, *International Journal of Scientific & Technology Research*, 2(5), pp. 268–274.

Pini Prato, G. and Cortellini, P. (2016). Thirty-year stability after regeneration of a deep intrabony defect: a case report. *Journal of Clinical Periodontology*, 43(10), pp. 857–862.

Pico-Blanco et al. (2016). Saving Single-rooted Teeth with Combined Endodontic-periodontal Lesions. *Journal of endodontics*, 42(12), pp.1859–1864.

Pretzl, B. et al. (2009a). Effort and costs of tooth preservation in supportive periodontal treatment in a German population. *Journal of Clinical Periodontology*, 36(8), pp. 669–676.

Pretzl, B.et al. (2009b). Guided tissue regeneration with bioabsorbable barriers III 10-year results in infrabony defects. *Journal of Clinical Periodontology*, 36(4), pp. 349–356.

Ricucci, D., Siqueira, J. and Rôças, I. (2021). Pulp Response to Periodontal Disease: Novel Observations Help Clarify the Processes of Tissue Breakdown and Infection. *Journal of Endodontics*, 47(5), pp. 740–754.

Rios, H. et al. (2015). Periodontal Wound Healing. *In:* Lang, N. and Lindhe, J. (Ed). *Clinical Periodontology and Implant Dentistry*. 6th ed. Chichester. Wiley Blackwell, pp. 521–535.

Roccuzzo, M. et al. (2010). Ten-year results of a three-arm prospective cohort study on implants in periodontally compromised patients. Part 1: implant loss and radiographic bone loss. *Clinical Oral Implants Research*, 21(5), pp. 490–496.

Rotstein, I. (2017). Interaction between endodontics and periodontics. *Periodontology 2000*, 74(1), pp. 11–39.

Rotstein, I., and Simon, J. (2004). Diagnosis, prognosis and decision-making in the treatment of combined periodontal-endodontic lesions. *Periodontology 2000*, 34, pp. 165–203.

Sculean, A. et al. (2008). Ten-year results following treatment of intra-bony defects with enamel matrix proteins and guided tissue regeneration. *Journal of clinical periodontology*, 35(9), pp. 817–824.

Sculean, A. (2017) Current clinical concepts in regenerative periodontal therapy. *Perio Insight, 5*.

Sanz, M. et al. (2020). Treatment of stage I-III periodontitis-The EFP S3 level clinical practice guideline. *Journal of Clinical Periodontology*, 47 Suppl 22(Suppl 22), pp. 4–60.

Simring, M. and Goldberg, M. (1964). The Pulpal Pocket Approach: Retrograde. *The Journal of Periodontology*, 35(1), pp. 22-48.

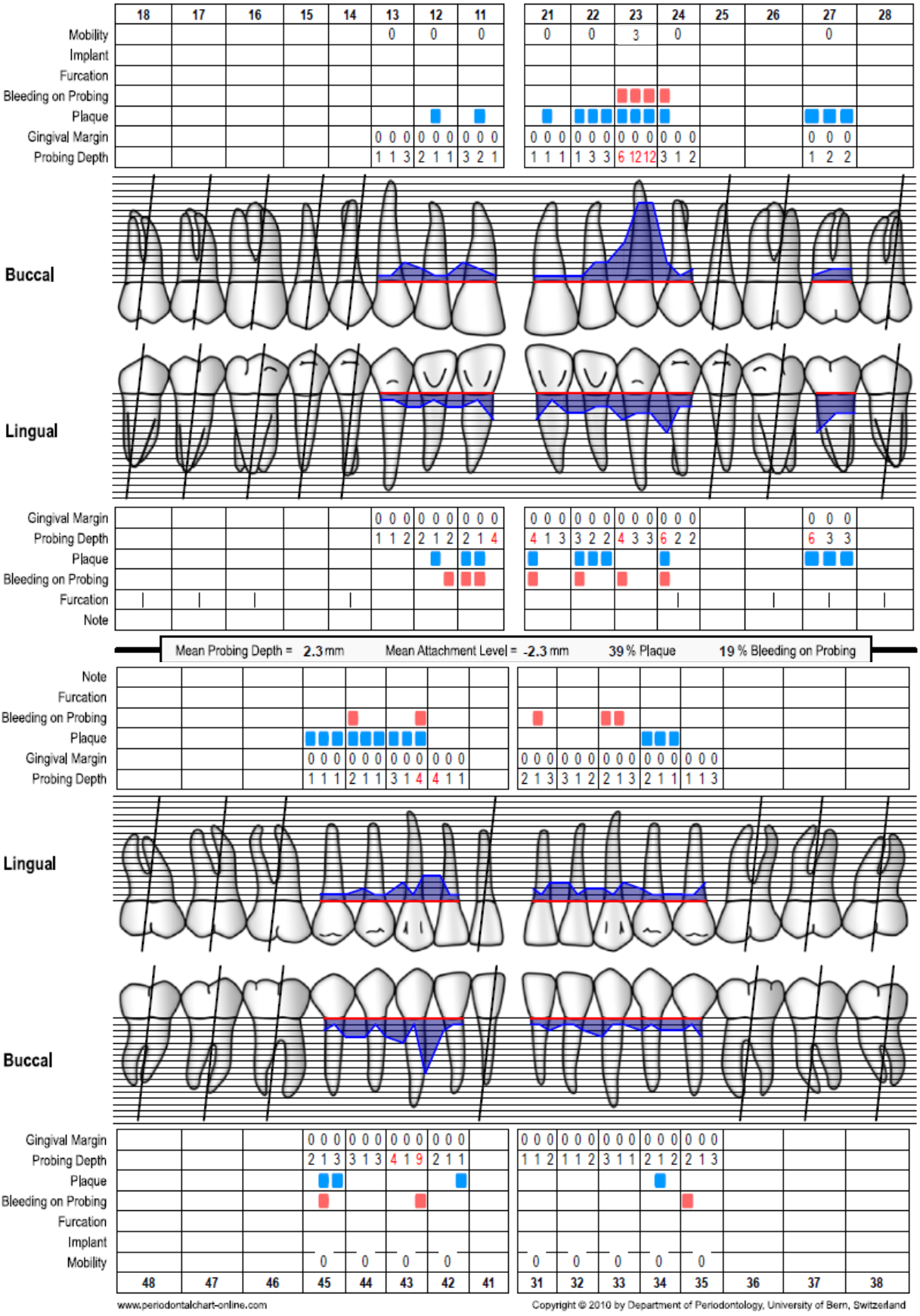
Turner, J. and Drew, A. (1919). An Experimental Inquiry into the Bacteriology of Pyorrhoea. Proceedings of the Royal Society of Medicine. *Royal Society of Medicine*, 12(Odontol Sect), pp. 104–118.

Wennström, J and Lang, N. (2015). Treatment Planning for Implant Therapy in Periodontally Compromised Patient. *In:* Lang, N. and Lindhe, J. (Ed). *Clinical Periodontology and Implant Dentistry*. 6th ed. Chichester. Wiley Blackwell, pp. 641–653.

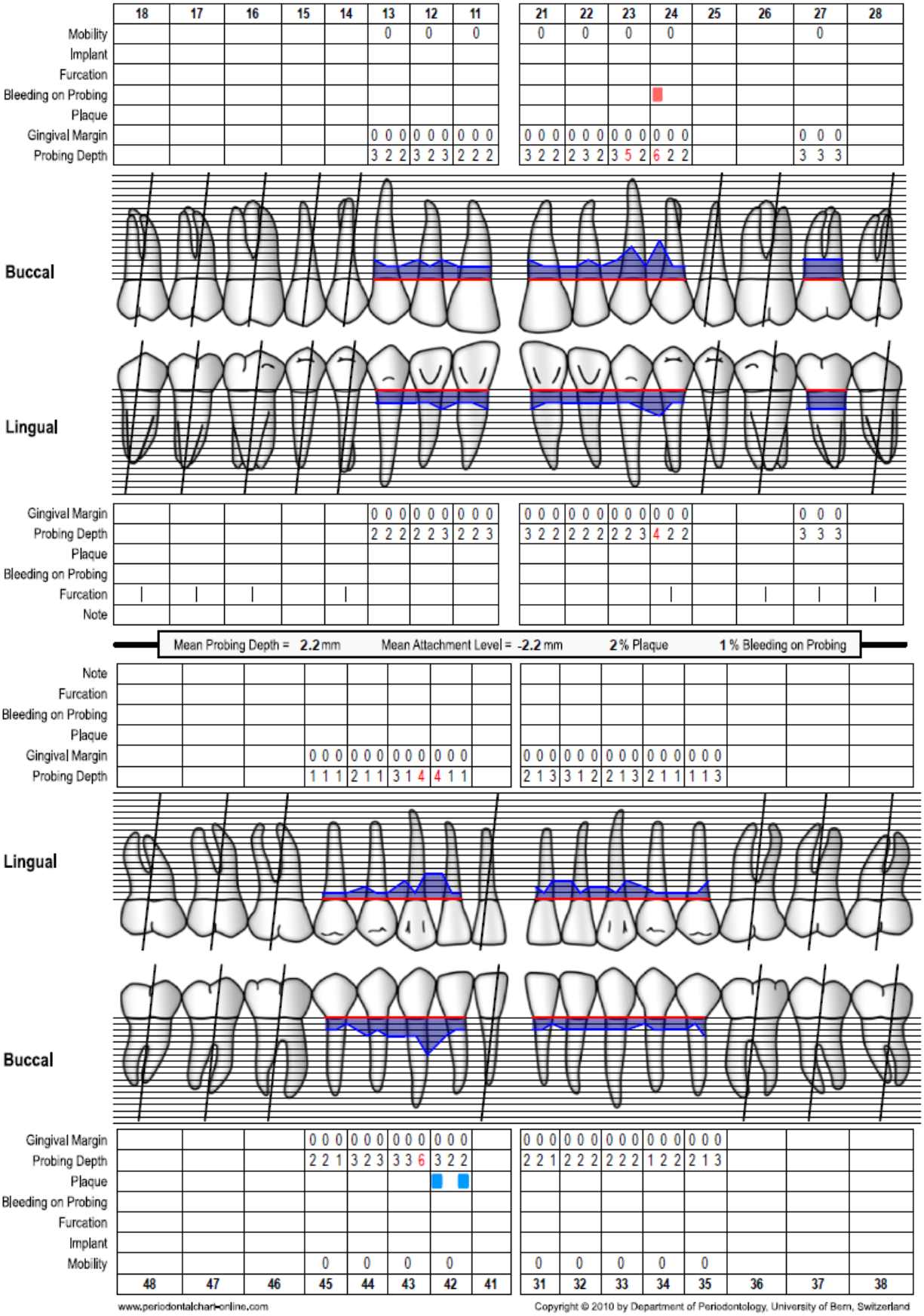
Zehnder, M., Gold, S. and Hasselgren, G. (2002). Pathologic interactions in pulpal and periodontal tissues. *Journal of Clinical Periodontology*, 29(8), pp. 663–671.

6 – Attachments

Attachment 1 – Initial Periodontogram



Attachment 2 – Re-evaluation Periodontogram



Attachment 3 – Assent of the Ethics Committee of Fernando Pessoa University

Universidade Fernando Pessoa

Exma. Senhora
Prof. Doutora Sandra Gavinha
Directora da FCS

Nº	Data
FCS/MED -176/21	12 de Maio de 2021

Exma. Senhora Professor Doutora,

A Comissão de Ética, depois de apreciado o projeto de investigação apresentado por Cláudia Isabel Pires Ferreira da Silva, intitulado "Periodontal regenerative therapy in endo-periodontal lesions: a case report", a realizar no âmbito do Mestrado Integrado em Medicina Dentária, considera o estudo muito pertinente. O objetivo do estudo é fazer a descrição de um caso clínico das Clínicas Pedagógicas de Medicina Dentária da Universidade Fernando Pessoa, mostrando e discutindo novos horizontes e soluções para as lesões endo-periodontais. Trata-se de um estudo qualitativo, nomeadamente, um caso clínico da Clínica Pedagógica de Medicina Dentária da Universidade Fernando Pessoa.
A aluna tem participado no atendimento clínico como assistente. Só se dará início ao estudo após obtenção de autorização da Direção das clínicas pedagógicas de MD - FCS-UFP, que será solicitada após obtenção do parecer desta Comissão. Ao longo do estudo não será revelado pelo investigador quaisquer dados que identifiquem o participante, mantendo assim o seu anonimato e todos os seus dados serão tratados de forma confidencial. Está também prevista a existência de um consentimento informado. O anonimato dos dados recolhidos está salvaguardado assim como é assegurado que a intervenção no âmbito deste caso clínico não coloca em risco o bem-estar do participante interveniente.

A Comissão de Ética não tem nada a opor à realização do estudo.

Com os melhores cumprimentos,

A Presidente da
Comissão de Ética da UFP

Teresa Toldy

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Attachment 4 – Informed Consent

Consentimento Informado

Declaro para os devidos efeitos legais, que autorizo a utilização dos dados, fotografias e imagens, sem nunca ser revelada a minha identificação, para o estudo conduzido no âmbito da Dissertação em Mestrado Integrado em Medicina Dentária da Faculdade de Ciências da Saúde da Universidade Fernando Pessoa, realizada pela aluna Cláudia Isabel Pires Ferreira da Silva, aluna nº 35016.

Mais declaro expressamente, que as referidas imagens e fotografias poderão ser utilizadas, alteradas e manipuladas em qualquer programa para o estudo ou publicação do mesmo, bem como poderão ser reproduzidas parcialmente, ou na sua totalidade, em qualquer suporte (papel ou digital), desde que seja garantida a confidencialidade dos dados bem como a minha identificação.

Estas imagens não poderão, em caso algum, ser cedidas a outrem sem expressa e prévia autorização minha.

Declaro ainda que me foi dada a oportunidade de obter esclarecimentos adicionais que considere necessários, assim como me foi comunicado o meu direito de me retirar do estudo a qualquer momento, sem prejuízo algum, presente ou futuro.

Por ser verdade, e por nada haver a obstar, esta declaração vai ser assinada por mim,

Porto, 23 de Março de 2021

Assinatura: [redacted]

Investigador Responsável: Cláudia Isabel Pires Ferreira da Silva

Assinatura: Cláudia Isabel Pires Ferreira da Silva