

Case Report

## PDH-MIX© PROTOCOL: CORRECT INSERTION OF IMMEDIATE IMPLANTS IN POST-EXTRACTION MOLAR SITES

F. Romano<sup>1</sup>, R. Scarano<sup>2</sup>, A. Frisone<sup>2</sup>, F. Tricca<sup>2</sup>, A. Scarano<sup>2\*</sup> and S.R. Tari<sup>2</sup>

<sup>1</sup>Private practice, Palermo;

<sup>2</sup>Department of Innovative Technologies in Medicine & Dentistry, University of Chieti-Pescara, Italy;

\*Correspondence to:

Prof. Antonio Scarano, D.D.S., M.D.

Department of Innovative Technologies in Medicine and Dentistry,

University of Chieti-Pescara,

Via Dei Vestini 31,

66100 Chieti, Italy

e-mail: ascarano@unich.it

### ABSTRACT

There is a widespread tendency in oral implantology that leads to consider the immediate post-extraction implant more frequently in the frontal region and, although less often, in posterior areas. Each of these sectors has its peculiarities, advantages, and risks. Although there are several shared protocols for the immediate post-extraction system in the front area, there are none for those in the rear sectors. The aim of this study is to propose, through the presentation of a case report, systematics that makes it as predictable to the clinician beforehand, in the diagnostic phase, to draw up a treatment plan as close as possible to the situation that will be found once the tooth has been extracted. That is, to give a technique, which in any case is always for experienced operators, for which the immediate insertion of the implant once the multi-rooted tooth has been extracted and its long-term success is more predictable.

**KEYWORDS:** *implant, fixture, protocol, bone, crest, alveolus*

### INTRODUCTION

There is a widespread tendency in oral implantology that leads to consider the immediate post-extraction implant more frequently in the frontal region and, although less often, in posterior areas. Each of these sectors has its peculiarities, advantages, and risks. Patients and operators agree in favoring less inquisitive solutions possible, fewer sessions, and therefore greater speed to reach the end of treatment in the shortest possible time, where the conditions are met.

Although there are several shared protocols for the immediate post-extraction system in the front area (1), there are none for those in the rear sectors. If it is true that some studies speak of high success rates (2, 3), others instead report a high possibility of failure linked to the diameter of the fixtures (4). A recent prospective study of 15 consecutive patients, in which 4 of 15 immediate post-extraction implants on molars had to be removed before 1 year, demonstrated a relatively low survival rate (73.3%) (5).

Received: 29 August 2023  
Accepted: 04 October 2023

Copyright © by LAB srl 2023 ISSN 2975-1276

This publication and/or article is for individual use only and may not be further reproduced without written permission from the copyright holder. Unauthorized reproduction may result in financial and other penalties. Disclosure: All authors report no conflicts of interest relevant to this article.

In any case, they are studies that exclude infected alveoli or cases in which fixtures "cannot" be inserted (due to poor quantity or quality of residual bone found in the surgical phase and not predictable by x-ray examination or pre-operative planning); therefore, these researches do not inform us about the predictability of the possibility of successfully inserting an immediate post-extraction implant into molar sites.

The studies of the reviews above mainly investigate the success rate, or survival, of those implants that have been able to be inserted because the anatomical situations of the post-extraction alveolus have been considered reliable. The problem of the clinician is, instead, being in front of the patient and not having yet extracted the tooth - therefore not knowing if and what anatomical conditions the post-extraction alveolus will present - predict in advance if in that case an implant can be inserted with the appropriate conditions of stability, correct positioning and asepsis, or an ARP (Alveolar Ridge Preservation) will have to be performed (6) and the insertion of the fixture will have to be postponed or postponed.

First, the patient must always be warned, not intraoperatively, to avoid uncomfortable situations, disappointments, or false expectations (7). In fact, the option of a second surgical phase should always be proposed in the first visit, possibly also giving the patient an idea of its greater or lesser percentage predictability. Even in the relationship of communication with the patient, these are relevant aspects (8).

In fact, it must be considered that several of these post-extraction sites could present (radiographically or clinically) infections or bacterial contamination due to infiltrations, fractures, and endo-periodontal lesions. These, when present, in addition to having to be naturally resolved and decontaminated, indirectly affect the quality and quantity of the residual alveolar bone and, therefore, the presence or absence of minimum conditions required to obtain the primary stability of the fixture, the correct positioning from the point of view and the possibility of safe healing of the site (9). It is, therefore, very difficult to predict whether the residual inter-radicular bone will be of adequate quality and quantity to accommodate the fixture in multi-rooted teeth in the immediate post-extraction phase. That said, it is up to the operator to use all available means to increase the chances of concluding the implant insertion in a single surgical phase (avulsion and immediate insertion of the fixture in the post-extraction alveolus)

In summary, the challenges that in this type of intervention we must face are:

- a) the preservation of bone, both of the buccal wall and the interradicular septum, that can be lost or compromised as a consequence of an inquiring avulsion, particularly in the frequent ankylosed elements;
- b) the correct management of the residual infection (from the odontogenic lesion, granuloma, or cyst), which is not an obstacle because it can and must be neutralized (10), but which certainly can increase the risk of contamination, and therefore of lack of osseointegration, of part or all of the implant surface (11). Systemic antibiotic therapy is not always sufficient to do this (12);
- c) the reliable closure by the second intention of the gap, almost always > 2 mm (13), which hesitates between fixtures and residual alveolar walls;
- d) stabilization of the clot, including adequate protection of the (14) flapless post-surgical site;
- e) the induction of healing by the second intention, aiming to maintain or increase the peri-implant keratinized gingiva band (15).

The aim of this study is to propose, through the presentation of a case report, systematics that makes it as predictable to the clinician beforehand, in the diagnostic phase, to draw up a treatment plan as close as possible to the situation that will be found once the tooth has been extracted. That is, to give a technique, which in any case is always for experienced operators, for which the immediate insertion of the implant once the multi-rooted tooth has been extracted and its long-term success is more predictable.

## CLINICAL CASE REPORT

### *Patient evaluation and case planning*

Female patient, 46 years old, non-smoker, good oral hygiene, general negative history. Radiographic examination revealed an encapsulated, fractured, asymptomatic 1.6 (Fig. 1, 2).

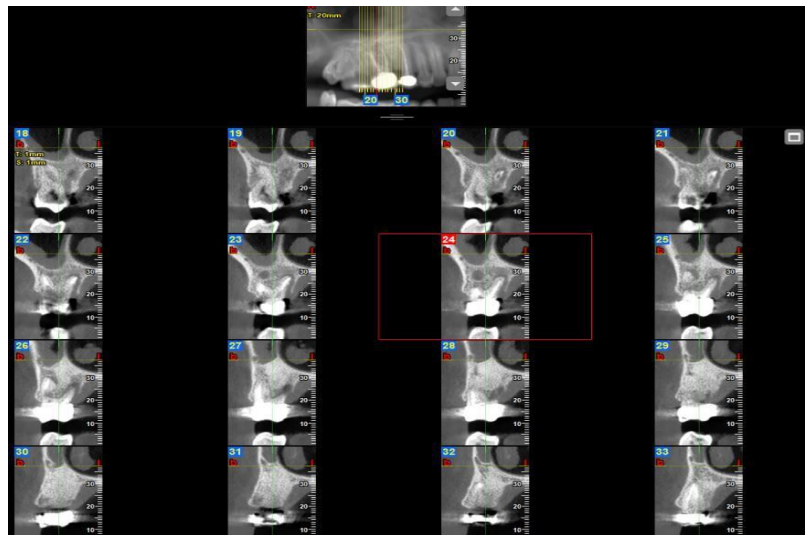


**Fig. 1.** Encapsulated, fractured, asymptomatic 1.6 pre op.

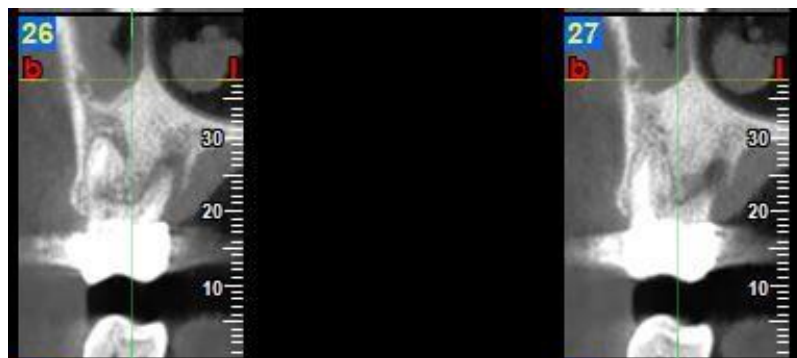


**Fig. 2.** Encapsulated, fractured, asymptomatic 1.6 rvg T=0.

The CBCT confirmed the presence of periapical odontogenic lesions organized on the two mesial and distal-vestibular roots (Fig. 3, 4) and helped analyze residual bone thicknesses and anatomical relationships with the maxillary sinus floor and surrounding tissues. Also, the thickness and conditions of soft tissue were evaluated and found stable.



**Fig. 3.** CBCT T=0.



**Fig. 4.** CBCT confirmed the presence of periapical odontogenic lesions organized on the two mesial and disto-vestibular roots.

### *Surgical procedure*

According to a known protocol, the patient was prepared for surgery and received complete mouth disinfection by the dental hygienist one week before surgery (16). She also received pharmacological protocol: Azitromicine 500 mg, 1 every 24 hours for three days, beginning the day before the surgery; paracetamol 1000 mg, 2 hours before surgery; chlorhexidine 0,20% rinse, 3 per day, from 3 days before surgery.

Two anesthetic cartridges (Mepi Mynol 20 mg/ml, mepivacaina cloridrato, 1:100.000) were injected locally from the beginning till the end of the surgery (50 min). These were the phases of surgery, as shown in the pictures:

1. Atraumatic avulsion. The alloy-porcelain crown, present in this case, is removed, and the rest of the clinical crown is separated (Fig. 5) following the root anatomy, with the normal tungsten carbide cutter separating the roots up to the floor of the pulp chamber.



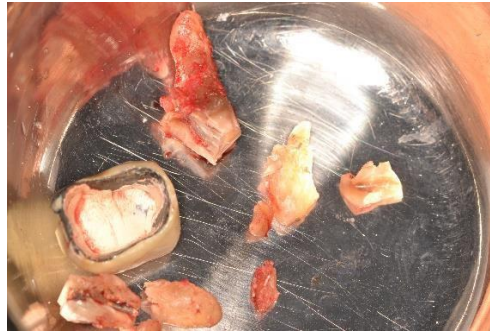
**Fig. 5.** *The alloy-porcelain crown is removed, and the rest of the clinical crown is separated.*

2. With a special piezoelectric insert (ES009NT, Esacrom<sup>®</sup>), the separation of the roots was completed with a conservative technique and in safety for the surrounding noble structures (floor of the maxillary sinus, bundle bone, palatine artery), reducing surgical times and post-operative morbidity for the patient (Fig. 6) (17).



**Fig. 6.** *Completed separation of the roots with a special piezoelectric insert (ES009NT, Esacrom<sup>®</sup>).*

3. The avulsion was particularly inquiring since the roots are ankylosed. Eight fragments were gently extracted with the utmost respect for the residual anatomy, preserving the maximum hard tissues that will provide primary stability to the fixture (Fig. 7).



**Fig. 7.** *Extracted fragments.*

4. *Decontamination and inspection of the post-extraction site.* The cavitation effect (18) is now adopted in its appearance as a powerful tissue decontaminator. It is exploited, even after removing the apexes and the granulation tissue present, leaving the insert (the same used for avulsion) to vibrate for 30-40 seconds inside the post-extraction alveolus filled with physiological saline solution (Fig. 8). The insert can be of any type; the important thing is that it does not come into contact with the alveolar bone tissue but is immersed and surrounded by saline solution (the recommended parameters for this procedure with this insert are  $U = 60$ ;  $V=90$ ;  $P=100$ ). The conservative technique used guarantees an excellent field visibility (due to the hemostatic effect of cavitation), and the maintenance of the most significant amount of alveolar bone possible, thanks to piezoelectric surgery (Fig. 9) (18).

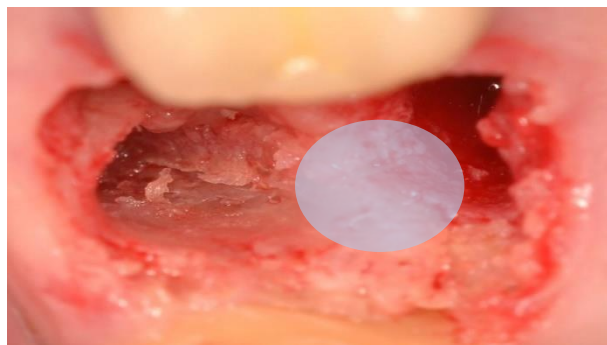


**Fig. 8.** *Post-extraction alveolus filled with physiologica.*



**Fig. 9.** *Result of the conservative technique.*

5. *Implant insertion.* Once the site for the placement of the implant has been identified with the piezoelectric handpiece (insert ES052XGT, Esacrom<sup>®</sup>) or similar, depending on the thickness of residual bone, the first invitation to osteotomy is gently practiced in the center of the interradicular septum bone (Fig. 10).



**Fig. 10.** Osteotomy area (with Piezo).

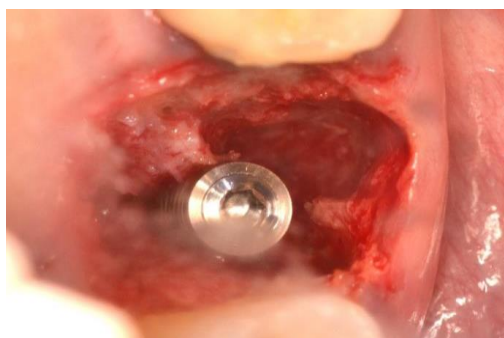
This is the most important cut, and the *Piezo* is the only tool capable of maintaining such thin thicknesses but also sufficiently resistant to accommodate the implant. This portion of the bundle bone will guarantee the necessary primary stability, Torque, and ISQ to the fixture that will be placed.

6. When this is done, it is easier to continue the osteotomy at low speed (250-300 rpm) with the implant kit's progressive cutters according to the different manufacturers' protocols (Fig. 11).



**Fig. 11.** After the initial drilling with Piezo, the osteotomy ends with the cutters of each implant kit.

7. After the osteotomy, the site is prepared or underprepared (in this case, a cutter Ø 3.5 mm), according to the quantity and quality of bone D1-D4 the fixture is inserted, in this case of Ø 4.1mm, with an insertion Tq 35 Nmc, and ISQ (Osstell<sup>®</sup>) 80-50 (Fig. 12).



**Fig. 12.** Implant correctly inserted in the residual bone.

8. *Hyaluronic Acid (H-mix).* xHYA Regedent<sup>®</sup>, a cross-linked stabilized Hyaluronic Acid gel, fills the gap in the alveolar bone. Everything is then stabilized by a collagen tablet (Collaplug; Zimmer<sup>®</sup>) placed coronally to protect

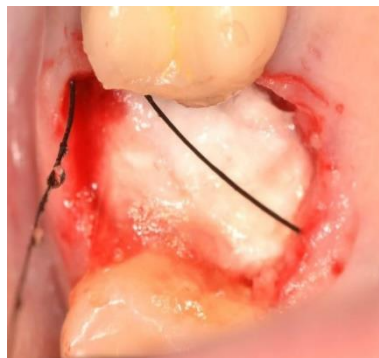
the site previously soaked with xHYA gel (Fig. 13). Although it has been shown that xHYA, both with collagen and without, still has a bone regeneration effect (19), it is preferable to use it for *space-making*, given the large crater formed after these teeth' extraction.



**Fig. 13.** Collagen tablet (Collaplug; Zimmer®) placed coronally to protect the site.

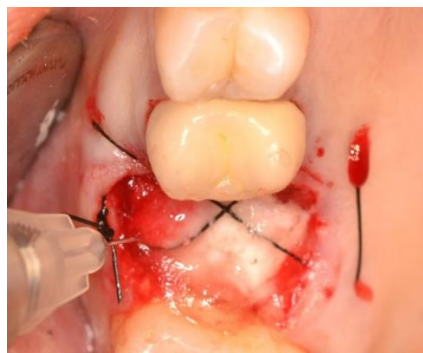
The procedure of mixing xHYA and Collagen aims to maintain its “space-making” effect for as long as possible, slowing down its reabsorption and lysis by salivary proteases (20), thus allowing a better stabilization of the clot and, at the same time, ensuring good healing for second intention.

9. *The suture.* A cross-stitch in pseudo-monofilament polyamide (*Supramid* n. 4/0) is given, with care to involve sufficient portions of healthy and thick tissues (Fig. 14). Healing by second intention creates the conditions for the increase of keratinized gingiva, fundamental for the success and long-term maintenance of peri-implant soft and hard tissues.



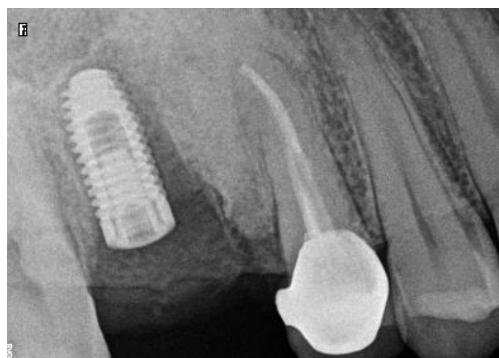
**Fig. 14.** The suture.

10. An additional application of xHYA is directed to cover the entire area (Fig. 15). It is necessary not to swallow the patient for 3-4 minutes to let the gel solidify and instruct him so that for the 2 hours following the operation he does not drink, eat or throw his mouth.



**Fig. 15.** Additional xHYA is inserted all over the graft.

11. Final RVG (Fig. 16).



**Fig. 16.** *Final RVG*

12. The following controls evidence the effectiveness of healing (Fig. 17-20).



**Fig. 17.** *Control at 7 days.*



**Fig. 18.** *Removal of the suture.*



**Fig. 19.** *Effectiveness of healing T=4m.*



**Fig. 20.** *Effectiveness of healing T=4m RVG.*



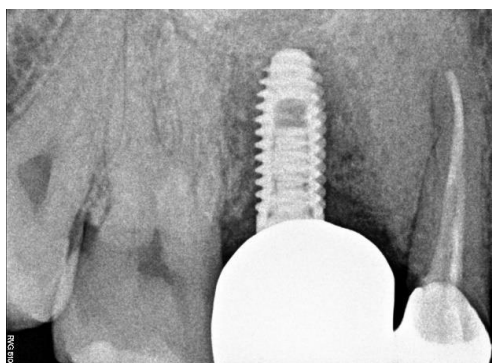
13. Delivery of the final work at 5 months (Fig. 21-24).



**Fig. 21.** Note the healed soft tissue around the implant.



**Fig. 22.** Final delivery of the ceramic.



**Fig. 23.** Final RVG T=5months.



**Fig. 24.** T=5 months; note the maintenance of a large band of KG.

## DISCUSSION

Piezoelectric surgery is an excellent tool to handle delicate or compromised hard- and soft-tissue conditions with less risk for the patient. Minimal accidental damage to adjacent soft-tissue structures allows for a safe and gentle surgical approach, particularly to thin and fragile bony structures (18, 21). Piezoelectric instruments reduce the risk of nerve damage when used for lower molar tooth extraction. When it is used in the upper posterior sites, it is safer when, as often happens, the clinician is working close to the maxillary sinus area or near the vase and nerves.

The reduction of overheating, frequent in extraction with classic instrumentation, bone surgery, or implantology, is explained by the generation of a *cavitation* effect in the irrigation solution due to the mechanical micromovements at a frequency of approximately 25–30 kHz. This also accounts for the local sterilization effect and reduced bleeding, which means better surgical visibility and increased safety (22, 23).

A mechanical shock wave that vibrates linearly produces the sonic and ultrasonic frequency (25-30 kHz). The cutting tip works with a reduced vibration amplitude (horizontal 20-200  $\mu\text{m}$ , vertical 20-60  $\mu\text{m}$ ). This allows for the main advantages of this device, which are precise and selective cutting, the avoidance of thermal damage, and safety for the patient (22). The selective cutting is the result of the limited amplitude. Only mineralized tissue will be cut at this amplitude because soft tissue requires frequencies greater than 50 kHz (24).

Resonance-frequency analysis was applied to evaluate the implant-stability quotient (ISQ) in sites prepared by conventional drilling or piezoelectric tips. It showed significant increases in ISQ values for the piezo-surgery group. Therefore, the ISQ of the fixtures placed using the piezoelectric device was greater than that obtained when the implants were placed using the conventional technique (25).

Several clinical studies have evaluated the degree of contamination of the autogenous bone particles that can be obtained with bone collectors during implant osteotomy. The result demonstrated that collected bone particles contain oral microorganisms that may cause infectious complications. Owned to the effectiveness of different decontamination methods, stringent aspiration protocol, preoperative oral chlorhexidine rinse, and antibiotic prophylaxis (26, 27) were important precautions that have been tried to implement when collected bone particles are to be implanted. Despite reducing contamination of collected bone particles, none of the methods described in the literature can completely decontaminate collected bone particles or prevent the risk of infectious complications. Further research is needed to identify more effective decontamination methods (28). The presented PDH-mix protocol is a proposal in that sense.

Hyaluronic Acid (HyA) is well known as a non-sulfated glycosaminoglycan structured biomolecule and a major natural component of the extracellular matrix in many tissues, including the skin (29), joints, eyes, and periodontium (30). The rationale for using it in PDH-mix protocol is because, physiochemically and biologically, HyA has been demonstrated to have huge effects: bacteriostatic (31, 32), antibacterial (33), anti-inflammatory (34) and anti-oedematous (30, 31). Moreover, extensive in vitro studies have demonstrated that HyA significantly stimulates clot formation (29, 35), induces angiogenesis (36), and increases osteogenesis (29, 37); all factors we strongly need to make more predictable the post-extractive immediate implant in the posterior area. Moreover, the piezoelectric device stimulated peri-implant osteogenesis and reduced proinflammatory cytokines (38).

All these factors, synergistically gathered in PDH-mix protocol, can provide a more reliable and predictable surgical placement of the implant in a fresh extraction socket, healthy and/or ankylosed or not, after molar extraction.

## CONCLUSIONS

Atraumatic extraction and immediate implant placement in the molar area is a challenging procedure for the clinic, and it's, in any case, for expert operators.

The PHD-mix protocol may improve the possibilities to insert the fixture and improve the prognosis relative to the final esthetic and functional results, facing the different local anatomical and biological situations and decreasing the complications, reducing the number of surgical procedures required to end the case successfully.

## REFERENCES

1. Buser D, Chappuis V, Belser UC, Chen S. Implant placement post extraction in esthetic single tooth sites: when immediate, when early, when late? *Periodontol* 2000. 2017;73(1):84-102. doi:<https://doi.org/10.1111/prd.12170>
2. Ketabi M, Deporter D, Atenafu EG. A Systematic Review of Outcomes Following Immediate Molar Implant Placement Based on Recently Published Studies. *Clin Implant Dent Relat Res*. 2016;18(6):1084-1094. doi:<https://doi.org/10.1111/cid.12390>
3. Atieh MA, Payne AG, Duncan WJ, de Silva RK, Cullinan MP. Immediate placement or immediate restoration/loading of single implants for molar tooth replacement: a systematic review and meta-analysis. *Int J Oral Maxillofac Implants*. 2010;25(2):401-415.
4. Atieh MA, Alsabeeha NH, Duncan WJ, et al. Immediate single implant restorations in mandibular molar extraction sockets: a controlled clinical trial. *Clin Oral Implants Res*. 2013;24(5):484-496. doi:<https://doi.org/10.1111/j.1600-0501.2011.02415.x>
5. Meijer HJA, Raghoobar GM. Immediate implant placement in molar extraction sites: a 1-year prospective case series pilot study. *Int J Implant Dent*. 2020;6(1):3. doi:<https://doi.org/10.1186/s40729-019-0201-7>
6. Canullo L, Pesce P, Antonacci D, et al. Soft tissue dimensional changes after alveolar ridge preservation using different sealing materials: a systematic review and network meta-analysis. *Clin Oral Investig*. 2022;26(1):13-39. doi:<https://doi.org/10.1007/s00784-021-04192-0>
7. Weller J, Boyd M, Cumin D. Teams, tribes and patient safety: overcoming barriers to effective teamwork in healthcare. *Postgrad Med J*. 2014;90(1061):149-154. doi:<https://doi.org/10.1136/postgradmedj-2012-131168>
8. Dartiguelongue JB, Cafiero PJ. Communication in health care teams. *Arch Argent Pediatr*. 2021;119(6):e589-e593. doi:<https://doi.org/10.5546/aap.2021.eng.e589>
9. Waasdorp JA, Evian CI, Mandracchia M. Immediate placement of implants into infected sites: a systematic review of the literature. *J Periodontol*. 2010;81(6):801-808. doi:<https://doi.org/10.1902/jop.2010.090706>
10. Chrcanovic BR, Martins MD, Wennerberg A. Immediate placement of implants into infected sites: a systematic review. *Clin Implant Dent Relat Res*. 2015;17 Suppl 1(e1-e16). doi:<https://doi.org/10.1111/cid.12098>
11. Alqutaibi AY. Limited Evidence Suggests that the Immediate Placement of Dental Implants Into Infected Sites Versus Noninfected Sites in the Esthetic Zone Show Comparable Clinical Results. *J Evid Based Dent Pract*. 2019;19(2):180-182. doi:<https://doi.org/10.1016/j.jebdp.2019.05.002>
12. Lodi G, Azzi L, Varoni EM, et al. Antibiotics to prevent complications following tooth extractions. *Cochrane Database Syst Rev*. 2021;2(2):CD003811. doi:<https://doi.org/10.1002/14651858.CD003811.pub3>

13. Seyssens L, Eeckhout C, Cosyn J. Immediate implant placement with or without socket grafting: A systematic review and meta-analysis. *Clin Implant Dent Relat Res*. 2022;24(3):339-351. doi:https://doi.org/10.1111/cid.13079
14. Del Fabbro M, Corbella S, Taschieri S, Francetti L, Weinstein R. Autologous platelet concentrate for post-extraction socket healing: a systematic review. *Eur J Oral Implantol*. 2014;7(4):333-344.
15. Sanz M, Schwarz F, Herrera D, et al. Importance of keratinized mucosa around dental implants: Consensus report of group 1 of the DGI/SEPA/Osteology Workshop. *Clin Oral Implants Res*. 2022;33 Suppl 23(47-55). doi:https://doi.org/10.1111/clr.13956
16. Jervoe-Storm PM, Eberhard J, Needleman I, Worthington HV, Jepsen S. Full-mouth treatment modalities (within 24 hours) for periodontitis in adults. *Cochrane Database Syst Rev*. 2022;6(6):CD004622. doi:https://doi.org/10.1002/14651858.CD004622.pub4
17. Maglione M, Bevilacqua L, Dotto F, Costantinides F, Lorusso F, Scarano A. Observational Study on the Preparation of the Implant Site with Piezosurgery vs. Drill: Comparison between the Two Methods in terms of Postoperative Pain, Surgical Times, and Operational Advantages. *Biomed Res Int*. 2019;2019(8483658). doi:https://doi.org/10.1155/2019/8483658
18. Stubinger S, Stricker A, Berg BI. Piezosurgery in implant dentistry. *Clin Cosmet Investig Dent*. 2015;7(115-124). doi:https://doi.org/10.2147/CCIDE.S63466
19. Shirakata Y, Imafuji T, Nakamura T, et al. Cross-linked hyaluronic acid gel with or without a collagen matrix in the treatment of class III furcation defects: A histologic and histomorphometric study in dogs. *J Clin Periodontol*. 2022;49(10):1079-1089. doi:https://doi.org/10.1111/jcpe.13694
20. de Brito Bezerra B, Mendes Brazao MA, de Campos ML, Casati MZ, Sallum EA, Sallum AW. Association of hyaluronic acid with a collagen scaffold may improve bone healing in critical-size bone defects. *Clin Oral Implants Res*. 2012;23(8):938-942. doi:https://doi.org/10.1111/j.1600-0501.2011.02234.x
21. Scarano A. Traditional Postextractive Implant Site Preparation Compared with Pre-extractive Interradicular Implant Bed Preparation in the Mandibular Molar Region, Using an Ultrasonic Device: A Randomized Pilot Study. *Int J Oral Maxillofac Implants*. 2017;32(3):655-660. doi:https://doi.org/10.11607/jomi.5342
22. Stubinger S, Landes C, Seitz O, Zeilhofer HF, Sader R. [Ultrasonic bone cutting in oral surgery: a review of 60 cases]. *Ultraschall Med*. 2008;29(1):66-71. doi:https://doi.org/10.1055/s-2007-963507
23. Scarano A, Carinci F, Lorusso F, et al. Ultrasonic vs Drill Implant Site Preparation: Post-Operative Pain Measurement Through VAS, Swelling and Crestal Bone Remodeling: A Randomized Clinical Study. *Materials (Basel)*. 2018;11(12). doi:https://doi.org/10.3390/ma11122516
24. Labanca M, Azzola F, Vinci R, Rodella LF. Piezoelectric surgery: twenty years of use. *Br J Oral Maxillofac Surg*. 2008;46(4):265-269. doi:https://doi.org/10.1016/j.bjoms.2007.12.007
25. da Silva Neto UT, Joly JC, Gehrke SA. Clinical analysis of the stability of dental implants after preparation of the site by conventional drilling or piezosurgery. *Br J Oral Maxillofac Surg*. 2014;52(2):149-153. doi:https://doi.org/10.1016/j.bjoms.2013.10.008
26. Salgado-Peralvo AO, Garcia-Sanchez A, Kewalramani N, et al. Consensus Report on Preventive Antibiotic Therapy in Dental Implant Procedures: Summary of Recommendations from the Spanish Society of Implants. *Antibiotics (Basel)*. 2022;11(5). doi:https://doi.org/10.3390/antibiotics11050655
27. Cornellini R, Scarano A, Covani U, Petrone G, Piattelli A. Immediate one-stage postextraction implant: a human clinical and histologic case report. *Int J Oral Maxillofac Implants*. 2000;15(3):432-437.
28. Tezulas E, Dilek OC. Decontamination of autogenous bone grafts collected from dental implant sites via osteotomy: a review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;106(5):679-684. doi:https://doi.org/10.1016/j.tripleo.2008.05.041
29. Pilloni A, Schmidlin PR, Sahrman P, Sculean A, Rojas MA. Effectiveness of adjunctive hyaluronic acid application in coronally advanced flap in Miller class I single gingival recession sites: a randomized controlled clinical trial. *Clin Oral Investig*. 2019;23(3):1133-1141. doi:https://doi.org/10.1007/s00784-018-2537-4
30. Eliezer M, Imber JC, Sculean A, Pandis N, Teich S. Hyaluronic acid as adjunctive to non-surgical and surgical periodontal therapy: a systematic review and meta-analysis. *Clin Oral Investig*. 2019;23(9):3423-3435. doi:https://doi.org/10.1007/s00784-019-03012-w
31. Dahiya P, Kamal R. Hyaluronic Acid: a boon in periodontal therapy. *N Am J Med Sci*. 2013;5(5):309-315. doi:https://doi.org/10.4103/1947-2714.112473
32. Pirnazar P, Wolinsky L, Nachnani S, Haake S, Pilloni A, Bernard GW. Bacteriostatic effects of hyaluronic acid. *J Periodontol*. 1999;70(4):370-374. doi:https://doi.org/10.1902/jop.1999.70.4.370
33. Eick S, Renatus A, Heinicke M, Pfister W, Stratul SI, Jentsch H. Hyaluronic Acid as an adjunct after scaling and root planing: a prospective randomized clinical trial. *J Periodontol*. 2013;84(7):941-949. doi:https://doi.org/10.1902/jop.2012.120269
34. Sasaki T, Watanabe C. Stimulation of osteoinduction in bone wound healing by high-molecular hyaluronic acid. *Bone*. 1995;16(1):9-15. doi:https://doi.org/10.1016/s8756-3282(94)00001-8
35. Scully MF, Kakkar VV, Goodwin CA, O'Regan M. Inhibition of fibrinolytic activity by hyaluronan and its alcohol ester derivatives. *Thromb Res*. 1995;78(3):255-258. doi:https://doi.org/10.1016/0049-3848(95)90876-h

36. West DC, Hampson IN, Arnold F, Kumar S. Angiogenesis induced by degradation products of hyaluronic acid. *Science*. 1985;228(4705):1324-1326. doi:<https://doi.org/10.1126/science.2408340>
37. Piloni A, Bernard GW. The effect of hyaluronan on mouse intramembranous osteogenesis in vitro. *Cell Tissue Res*. 1998;294(2):323-333. doi:<https://doi.org/10.1007/s004410051182>
38. Preti G, Martinasso G, Peirone B, et al. Cytokines and growth factors involved in the osseointegration of oral titanium implants positioned using piezoelectric bone surgery versus a drill technique: a pilot study in minipigs. *J Periodontol*. 2007;78(4):716-722. doi:<https://doi.org/10.1902/jop.2007.060285>