Allografts have been routinely used for immediate grafting of extraction sites as modalities of alveolar ridge preservation (ARP). Solvent-dehydrated bone allograft (SDBA), which is commonly utilized for socket grafting, exists in the form of cortical and cancellous particles. This study aims to provide a histologic comparison of cortical and cancellous SDBA for ARP. A total of 35 extraction sockets were allocated to receive either a cortical (17 sites) or cancellous (18 sites) SDBA, followed by application of a resorbable collagen wound dressing in both groups. At approximately 4 months, a bone core biopsy sample was obtained during implant placement. Histomorphometric assessment was then conducted to compare the differences between both forms of SDBA. Within its limitations, a higher percentage of vital bone was observed in the cortical bone group compared to the cancellous bone group (28.6% vs 20.1%, respectively, \( P = .042 \)), while there was a lack of statistically significant differences among other fractions of the bone biopsy sample (residual graft particles and nonmineralized tissues such as connective tissue or other components). Int J Periodontics Restorative Dent 2022;42:215–223. doi: 10.11607/prd.5563
for ARP amongst clinicians. The underlying Tutoplast process of this allograft is said to enhance its osteoconductive properties due to the preservation of the bone trabecular pattern, its porosity, and the mineralized composition. Nonetheless, when opting for SDBAs, clinicians may also face a dilemma between the selection of cortical or cancellous particles for grafting the extraction socket. While the healing of cancellous and cortical bone has been described for some allografts, to the best of the present authors’ knowledge, no study has yet investigated the difference in histologic performance when comparing a cortical to cancellous SDBA in socket grafting. Therefore, the aim of this study was to perform a histologic assessment of extraction sockets treated with a cortical vs cancellous SDBA and to assess the relevant factors in the formation of vital bone.

**Materials and Methods**

**Study Design and Patient Selection**

The present investigation was designed as a prospective clinical study. Healthy adults were recruited from a private practice in Italy if they presented with at least one nonrestorable tooth in need of extraction and future fixed-prosthesis implant restoration.

Subjects were not included in the study if any of the following factors were present: (1) an extraction socket that exhibited severe loss of the buccal plate after tooth extraction (> 50% dehiscence); (2) reported smoking habit of ≥ 10 cigarettes per day; (3) pregnancy; and (4) any medical condition or medication known to alter soft/hard tissue healing (poorly controlled diabetes mellitus, bisphosphonates therapy, immunosuppressives, etc).

After fulfillment of the inclusion criteria and thorough explanation of the study protocol, patients were asked to provide informed consent prior to recruitment. The present research was conducted in full accordance with ethical principles, including the Declaration of Helsinki of 1965, as revised in Tokyo in 2004, and approval by the local ethic committee.

**Surgical Protocol**

All procedures were carried out by the same experienced clinician (C.S.) and performed uniformly for all recruited participants, as done for previous studies. Briefly, after successful administration of local anesthesia, a no. 15C blade was used for detaching the supracrestal gingival fibers in the periodontal ligament space. The tooth was luxated with elevators and gently extracted with forceps. Care was taken to perform the extraction as minimally invasive as possible to preserve the buccal plate, which was recorded after extraction and categorized into either a thickness of < 1 mm or ≥ 1 mm using a periodontal probe (UNC-15, Hu-Friedy). In case of a molar extraction, the crowns were sectioned using a long slender fine diamond bur to remove the roots individually, if necessary. The socket walls were then examined for the presence of a fenestration or dehiscence and were thoroughly degranulated. If the socket exhibited > 50% loss in any of its walls, the extraction site was not included in the study, but the patient nonetheless received treatment using a guided bone regeneration approach.

The socket walls were scraped with a curette to induce bleeding and then densely packed to a level of 1 mm below the bone crest with either a cortical or cancellous SDBA (Puros Particulate Allograft, Zimmer Biomet). The allocation of the biomaterial per patient was randomly selected on a rolling basis after recruitment. A bioresorbable collagen wound dressing (Zimmer Collagen Plug, Zimmer Biomet) was gently placed to cover the grafted socket, and the site was secured using 4-0 absorbable sutures (Vicryl, Ethicon, Johnson & Johnson) in a cross-mattress technique. No attempt was made to obtain primary wound closure. Figure 1 presents an example of the surgical procedure.

After completion of the surgical procedure, patients were provided with complete postoperative instructions, which consisted of antibiotics (500 mg amoxicillin for 7 days, three times daily; or, in case of allergy, six 250-mg Zithromax tablets [two tablets for the first day, then one tablet for each
of the remaining 4 days), and anti-inflammatory medication (as indicated). Patients were also asked to rinse with warm salt water before switching to a twice-daily rinse with 0.2% chlorhexidine gluconate solution for 2 weeks (until the postoperative appointment), at which time the sutures were removed.

Fig 1  Example case of an extraction site treated with ARP using an SDBA. (a) Preoperative radiographic images (panoramic and cross-sectional views) of a CBCT scan. (b) Application of bone graft material and collagen dressing after standard tooth extraction, secured with 4-0 Vicryl sutures. (c) Clinical view of the extraction site at the early healing phase, immediately after suture removal (2 weeks). (d) Clinical view 4 months after ARP (e) Healing of the treated site immediately after flap elevation, prior to implant placement. (f) A bone core biopsy sample was harvested for histologic analysis. (g and h) Insertion of an appropriate implant after a bone core biopsy sample was obtained. (i) Periapical radiograph after provisionalization. (j) Lateral and (k) facial views of the treated site with the final restoration in place (1 year postoperative, in this example).
Reentry Procedure and Implant Placement

The patients were scheduled for implant placement after allowing for an undisturbed healing period of at least 4 months, at which point they returned for implant placement and harvesting of the bone core biopsy sample. At this stage, a mucoperiosteal flap was reflected and the sites were examined. Next, according to the position of the future implant, a bone core was harvested using a surgical trephine bur drill with either (1) an external 4.0-mm diameter and internal 3.0-mm diameter, or (2) a 3.0-mm external diameter and 2.0-mm internal diameter (Stoma). The bone core was harvested under saline irrigation at 600 rpm (up to 10 mm) to collect specimens before implant insertion (Tapered Screw-Vent, Zimmer Biomet). If deemed necessary, additional bone augmentation was also performed at the time of implant placement. All patients were seen approximately 2 weeks postoperatively, and the final restoration was fabricated according to the treatment plan within a 1-year period.

Histologic Processing and Histomorphometric Analysis

The harvested bone cores were removed from trephines and immediately placed into a buffered formalin solution (Sigma-Aldrich). The cores were dehydrated, polymethyl methacrylate-embedded, and serially segmented to obtain two sets of sections, thick (100 µm) and thin (5 µm), for the morphologic and the histomorphometric evaluations, as reported elsewhere. Thick sections were microradiographed (3K5, ItalStructures), while thin sections were stained with toluidine blue or Gömöri trichrome stain.

Examinations and photographs of the stained sections and the microradiographs were performed with a standard setting using a microscope under ordinary or polarized light (Axiophot, Zeiss). Analyses allowed quantification of the mineral component comprised of vital bone (as the presence of osteocytes in lacunae) and residual graft particles (regions of lamellar bone presenting lacunae without osteocytes) and quantification of the nonmineralized tissue components (connective tissue [CT]/others, including vasculature, loose fibrous CT, and inflammatory cells) per total tissue volume in order to obtain the percentages of each component from the harvested cores. The morphometry of images was performed using a suitable software (AnalySIS, Olympus Soft Imaging System).

Data Analysis and Visualization

For both groups of cortical and cancellous SDBA, means and SDs were calculated for the percentages of vital bone, residual graft particles, and CT/others tissues. For statistical comparison of the histologic components between the cortical and cancellous groups, a mixed-modeling regression approach was used to include fixed co-variates, such as time and the thickness of buccal plate, and a random effect for subject. Confidence intervals (CIs) were produced, and a P-value threshold of .05 was set for statistical significance. Additionally, box plots were produced to visualize the observed histologic outcomes. The analyses were conducted in Rstudio (version 1.3.1093), and the plots were produced using the ggplot2 package.

Results

Thirty-one patients were consecutively enrolled and received treatment. Three extraction sites were excluded from this analysis due to exhibiting > 50% loss of the buccal plate. As a result, a total of 28 patients (14 women, 14 men), and 35 treated extraction sockets were included in this study (18 sites allocated to the cancellous group, and 17 sites to the cortical group).

All surgical procedures related to the extraction, ARP, and implant placement were completed without complications, and bone core biopsy samples were harvested successfully from all included sites. No dropouts occurred. The mean time between ARP and biopsy sample harvesting/implant placement in the cortical and cancellous groups was 4.8 ± 1.1 months and 4.3 ± 0.82 months, respectively (P > .05). The average age of the recruited patients at the time of enrollment was 52.51 ± 8.22 years (52.3 ± 8.9 years for the cortical group; 52.6 ± 8.1 years for the cancellous group). While almost all of the treated sites pertained to the maxillary arch in both groups (100% of the sites in
the cortical group; 88.8% of sites in the cancellous group), the cortical group comprised significantly more posterior sites than the cancellous group (100% vs 50%, respectively). Additional details on patient characteristics and distribution of extraction sites according to the allocated SDBA are presented in Table 1.

Figure 2 shows the side-by-side comparison of the histomorphometric results of the cortical and cancellous SDBA groups in terms of vital bone, residual graft particles, and nonmineralized tissues (CT/other). The total amount of mineralized tissues per group ranged from 29.9% to 71.2% (mean: 46.1%) in the cortical group, and from 21.26% to 63.5% (mean: 38.8%) in the cancellous group. The average amount of identified vital bone varied among the two groups (28.6% for the cortical group, 20.1% in the cancellous group), and these differences reached statistical significance in the regression model (coefficient of cortical group: 8.6) (95% CI: 0.21, 16.9; P = .042).

The amount of residual graft particles in the cortical and cancellous SDBA groups presented as 17.4% ± 9.6% and 20.1% ± 12.2%, respectively, without statistically significant intergroup differences. Lastly, for the amount of nonmineralized tissues, the model did not present a statistically significant difference between the two groups (54.1% vs 59.8% for the cortical and cancellous sites, respectively). Additionally, with regard to the investigated factors, there was no significant relationship in the model between the variables of site (relative to molar vs nonmolar; model coefficient for molars: –4.43 [95% CI: –15.51, 6.64; P = .43]), sex (coefficient for men: –2.43 [95% CI: –13.11, 8.24; P = .68]), time (0.93 [95% CI: –3.29, 5.15; P = .66]), or the binary variable of buccal plate (< 1 mm thickness: –3.03 [95% CI: –11.33, 5.26; P = .47]) and the amount of vital bone.

Figure 3 shows histologic sections of cortical and cancellous treated sites, identifying new vital bone trabeculae and remaining graft particles surrounded by the fibrous tissue.

**Discussion**

Most of the published literature in the topic of ARP focuses on dimensional changes that occur after tooth loss as a result of unassisted healing, or the attenuation patterns through different therapeutic modalities. These primarily include investigating linear dimensional alterations in the horizontal (width) and/or vertical (height) component of the alveolar ridge. In this regard, most clinical studies and systematic reviews have reached the same conclusion that while postextraction ridge atrophy can be significantly reduced with ARP, the physiologic remodeling process after tooth loss cannot be completely eliminated. Studies have also investigated the histologic outcomes after ARP, namely the quality of bone at the time of implant placement. This is due to the notion that a higher percentage of vital bone can enhance ridge preservation and may be beneficial for long-term maintenance of peri-implant health or for accelerating the point at which implants achieve stability.

Several studies have assessed the healing of allografts through...
However, to the present authors’ knowledge, a direct assessment of cortical vs cancellous form of SDBA for socket grafting has not yet been performed. Thus, a direct comparison of the present results to the literature may not be feasible. Eskow and Mealey\textsuperscript{22} conducted the first human study to compare the clinical (ridge preservation) and histologic (bone quality) outcomes of a cortical and cancellous freeze-dried bone allograft (FDBA) for socket grafting that was sealed by a resorbable collagen dressing, similar to the present design. After an average healing time of 4.5 months, despite observing higher amounts of mineralized component and higher percentages of vital bone for their cortical group (16.08%, vs 12.98% for the cancellous group), the authors stated that the difference between the two groups had not reached statistical significance. Aside from differences in study design, setting, and population between the reference report\textsuperscript{22} and the present study, it may be speculated that the utilization of a SDBA in the current report may have contributed to a slightly higher percentage of vital bone. In fact, the same research group conducted a randomized clinical trial comparing the histologic outcomes of cancellous FDBA vs SDBA for ARP and observed a slightly higher percentage of vital bone for the SDBA-treated group at 3 months (24%, vs 27% for cancellous SDBA).\textsuperscript{17} When observing the relatively lower percentage of 20% vital bone in the present study’s cancellous SDBA group, it should be noted that the reference study\textsuperscript{17} reportedly utilized a barrier membrane to cover the grafted sockets, whereas the present study design comprised the application of a resorbable collagen dressing (which lacks compartmentalization properties) and may have resulted in slightly lower amounts of vital bone. Furthermore, similar to the present analysis, the study by Corning and Mealey also did not find a correlation between the percentage of vital bone and the thickness of the buccal plate, nor with tooth location or smoking habits.\textsuperscript{17} While the thickness and integrity of the buccal plate has been emerging as a strong predictor of postextraction dimensional ridge alterations,\textsuperscript{11,14} its precise correlation to histologic outcomes (bone healing) remains unclear. Nevertheless, it has to be mentioned that in the present study, the assessment of the buccal plate was performed dichotomously (as < 1 mm or ≥ 1 mm) using a periodontal probe.

\begin{figure}
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\includegraphics[width=\textwidth]{Fig2}
\caption{Box plots representing the numerical values of the histomorphometric results: percentages of nonmineralized tissues (CT or others), residual graft particles, and the relative amount of vital bone for the cortical and cancellous SDBA. The horizontal line dividing each box marks the median. Vertical lines extending outside the boxes indicate variability outside the quartiles. Individual observations in the dataset are presented with smaller rhomboids on top of each corresponding box. Note that no inference to statistical testing or comparison among the two groups is presented in this plot. The analyses were conducted in a mixed model to account for other co-variates.}
\end{figure}
Limitations of the present study are to be considered when interpreting the results. While the notion of a statistically significantly higher fraction of vital bone may seem attractive to readers, in the context of patient care, the clinical value of this difference is yet to be elucidated. This draws attention to the debate of clinical vs statistical significance. Readers should bear in mind that the difference in the average

Fig 3 Histologic sections of (a and b) cortical and (c and d) cancellous treated sites showing new vital bone trabeculae (VB) and remaining graft particles (RG) surrounded by the fibrous tissue. (a) Microradiograph. Scale bar = 500 µm. (b) Vital bone is present with osteocytes in lacunae, and osteoblasts (arrows) can be seen on bone surfaces. Toluidine blue stain. Scale bar = 100 µm. (c) Section of a bone trabecula stained by Gomori trichrome method under ordinary light. Scale bar = 500 µm. (d) Lamellation of the newly formed bone can be seen in the same sample as Fig 3c, shown here under polarized light.
percentage of vital bone among the two SDBA groups, while reaching a statistically significant difference of 8.5%, is merely indicative of the consistency of the present data and the results relative to the treated population. The actual impact of this difference in the context of clinical care (clinical significance) is not yet clarified in the literature. In this scope, long-term follow-up studies are needed to evaluate the pertinence of increased proportions of histologic components after ARP, specifically in the context of marginal bone level stability, maintenance of peri-implant health, and prevention of peri-implant disease or an effect on its treatment.27,28 Lastly, as previously mentioned, this is the first study to report on a direct comparison of cortical vs cancellous SDBA for socket grafting and ARP. Therefore, future high-powered trials are needed to verify these results.

Conclusions

Within the limitations of the present report, the results indicate that utilizing a cortical SDBA compared to a cancellous SDBA may lead to greater amounts of vital bone.

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