

Retrieval and Analysis of Explanted and In Situ Implants Including Bone Grafts

Jack E. Lemons, PhD

KEYWORDS

- Retrieval and analysis • Dental implants
- Histology histomorphometry

INTRODUCTION

Brief History

The retrieval and analysis of surgical implant devices as an integral component of academic research was expanded in the United States after an initial cosponsored consensus conference in the 1970s.¹ Guidelines developed at that meeting progressed to more standardized procedures, thereby permitting data exchanges at multiple levels within the profession.^{2,3} Subsequent consensus conferences expanded the details of information to be collected and clearly demonstrated the values of multidisciplinary studies for improving existing and developing new devices and procedures to enhance clinical outcomes associated with surgical implant devices.⁴⁻⁶

In Vitro Plus Laboratory and Human Specimens

Most implant device-oriented research, development, and applications initiate from an idea and in vitro laboratory studies to determine the physical, mechanical, chemical, electrical, and biologic (biocompatibility) properties of a device. In each situation, these studies are specific for the proposed clinical application. This is done to determine the initial safety of the intended clinical applications. Subsequent directed studies to evaluate efficacy extend to laboratory in vivo simulations for host biocompatibility interactions that includes function and preliminary human clinical

trials that are based on detailed protocols developed from the prior studies. One benefit of human retrieval and analysis (revision surgery or post mortem) investigations is the opportunity to compare, retrospectively, the pre- and postconditions of the device and host environment, including information from the actual human applications. This has been a theme within most device and retrieval programs and these types of programs now exist throughout the world.

Local Experience Since the 1970s

The program (University of Alabama at Birmingham [UAB]) discussed in this article was initiated in the early 1970s. The central theme was to investigate tissue and device interfaces and the conditions of transfers specific to synthetic origin elements from the device (biomaterials) and associated forces from the host associated with device function (biomechanics). This program was jointly based on UAB's schools of dentistry, medicine, and engineering and from the outset was interdisciplinary. It was realized that factors from patients, the technology of surgery and restoration, and the device should be separated using the expertise from those trained in the biologic, clinical, and physical sciences. This team concept was carried forward to regular meetings of all involved. The central foci of these meetings have been what has caused the need for this revision surgery (removal of the device) and what might have

Departments of Prosthodontics, Surgery and Biomedical Engineering, Schools of Dentistry, Medicine and Engineering, University of Alabama at Birmingham, 1530 Third Avenue South, SDB Box 61, Birmingham, AL 35294-0007, USA

E-mail address: jack.lemons@ortho.uab.edu

Oral Maxillofacial Surg Clin N Am 22 (2010) 419-423

doi:10.1016/j.coms.2010.06.002

1042-3699/10/\$ - see front matter © 2010 Elsevier Inc. All rights reserved.

been done to minimize this type of clinical outcome.

It was recognized that observations on the devices per se could be reported with confidence; however, overall cause-effect relationships often required testing of hypotheses. We called this approach forensic discovery. Over time and experience, thousands of specimens have been collected, leading to graduate student MS and PhD theses and dissertations, resident-based studies, and investigations focused on interests of faculty members. Often, studies have been based on single observations or, confirming or not, observations of others. In all situations, a concern has been the statistical significance from a clinical perspective, especially related to the numerator (number studied) versus the denominator (number used clinically). Specific to device properties, multiple examples exist where studies based on retrieval and analysis have confirmed that an initial observation would result in expanded interactions and, in some cases, these represented a larger number (thousands of devices). Thereby the overall outcome was a circumstance of statistical and clinical significance.

Current and Future Opportunities

As discussed previously, recognition of value associated with appropriate studies of explanted and in situ postmortem surgical implant devices has resulted in expansion of national and international programs. Another aspect is the opportunity to combine with existing and evolving clinical registries concerned with device outcomes, which should further enhance correlations of device-specific studies with expanded and detailed clinical records. We anticipate the evolution of regional, national, and international networks for information exchange based on secure Internet and Web systems. Key to this approach will be exchanges earlier in the cycles of device clinical applications while protecting the rights of all stakeholders.

MATERIALS AND METHODS

Summary of Experience for Identifying, Removing, Transferring, Receiving, Recording, Analyzing, and Reporting for Different Sources and Types of Specimens

Retrieved implant specimens for detailed analyses have originated from several sources. Studies of the preclinical specimens from university-based laboratory in vitro and in vivo investigations have provided the instrumentation, techniques, and

experience for subsequent analyses. Human specimens from revision surgeries include devices that are removed and replaced by another device and are called clinical failures. In contrast, those from postmortem donors that are in situ at the time of donation are called clinical successes. To analyze and compare results, records and details are obtained from protocols based on national and international standards.^{2,3}

In clinic-to-laboratory transfers, specimens are normally placed in containers with 10% buffered formalin, following procedures similar to tissue processing for pathology studies. At UAB, device specimens are transferred through the Department of Pathology, and retrieval and analysis programs treat the device as one part of evaluations (physical aspects of the device) needed to enhance patient care. All aspects of study fall under institutional review board (IRB)–and Health Insurance Portability and Accountability Act (HIPPA)–approved protocols. Off-site specimens must also include patient and clinician approvals for studies plus nationally approved packaging and transferring procedures. The UAB program has developed a minimum data set (a form) for information to be collected and transferred with each “general” type of specimen. On receipt, all specimens are initially treated as contaminated by infectious agents and all handling is conducted to assure safety and no or minimal damage to avoid altering as-received device and tissue conditions. This step often requires information exchange with the clinical investigator. To assure confidentiality, all explanted specimens are identified with a code IXXX with sequential numbering. After careful and appropriate observation and removal of loose debris, the specimens move to a triage step where they are separated into tiers I, II or III. Most specimens that are tier I represent conditions where all observations are “as anticipated” and specimens are moved to secure storage; tiers II and III are when something “unanticipated” is noted and these specimens are transferred to a group meeting for more detailed considerations.

The group meeting includes all interested parties where students include undergraduate and graduate levels, clinical residents, staff, and faculty. All meet together to observe and comment. The clinical participants present the patient and treatment information (including available radiology and pathology studies) whereas the nonclinical participants present the physical (engineering) aspects of the device and associated instrumentation. These discussions often result in hypotheses about what might have caused the unanticipated features and what studies might

provide answers. Protocols, studies, and peer-reviewed publications develop from this initial step. Tier II represents unanticipated alterations of the device, tissues, or related information where specimens are judged not to have influenced the clinical outcome. Tier III represents the more in-depth studies where the device or associated technology could have influenced the need for revision surgery. One special aspect of device and tissue studies related to biomaterial and biomechanical properties is the extensive instrumentation, test machine, and analytical analysis systems required to develop quantitative data. Additionally, because studies often focus on the implant-to-tissue interface, a fully equipped histology/histomorphometry laboratory, including nondecalcified and implant sectioning (Exakt) equipment, has developed to evaluate these types of specimens.

Postmortem en bloc device and host tissue specimens from individuals donating for research have provided opportunities to evaluate “nonrevision—called success” conditions. We call this a successful device and application representing in-place and in-function condition at the time of donation. Processing through tissue and organ donation facilities (a partner) facilitates this type of activity (a program started locally in 2005).⁷

Responsibilities for Information Collection and Dissemination

Current local, national, and international guidelines require that retrieval and analysis follow IRB and HIPPA rules and regulations. Although most device retrieval and analysis programs have operated under conditions of information control and nationally standardized procedures, annual review and approval of all participants is now a formal requirement within universities receiving contracts and grants. Our experience over past years is that this component of the studies requires approximately one full-time equivalent of investigator time.

Methods for Three Dental Studies

Three recent dental-oriented activities have been selected for presentation as examples of retrieval and analysis investigations.

Example one: bone implant contact for a root form design

A single design of root form dental implant, that was judged nonrestorable for replacement crowns by one dentist, was removed by surgical trephine, after permission for research study.⁸ Approximately 100 single units were removed over 3 years

from this practice site, placed in 10% buffered formalin, and transferred with records for graduate student studies. Stereomicroscopic examinations were used to select 49 candidates where bone along the implant was adequate for midline nondecalcified sectioning. This included Exakt system thin sections, staining with Sanderson red bone stain, and measurement of bone integration using optical microscopy and a Bioquant image analysis system.

Example two: Micro-CT of bone grafts

Patients with edentulous posterior maxillary regions were treated by a sinus lift surgical procedure, which included a calcium phosphate particulate mixed with patient blood as a bone graft.⁹ After 30 days, a central region of the implanted bone was removed by surgical trephine to provide a 4 × 8-mm core as a part of root form dental implant placement. Procedures were done at a single dental office and after approvals; the specimens fixed in 10% buffered formalin were transferred for graduate student studies focusing on micro-CT-based analyses. Specimens were removed from the trephine, oriented for processing, and CT imaged using a university-based micro-CT system. Analysis planes for CT were set at 7- and 20- μ m dimensions.

Example three: bone implant contact for a custom osseous integrated implants with particulate bone grafting

Three female patients were treated with implant reconstruction of edentulous mandibles that were subsequently donated for postmortem investigations.¹⁰ Implants were placed in 10% buffered formalin and, with permissions and records, transferred for graduate student studies. After radiographic imaging, six nondecalcified transverse sections were made along left and right distal and along four percutaneous post locations. Nondecalcified thin sections were prepared and analyzed for bone implant contact (BIC) and other bone properties as for the root form devices (discussed previously).¹⁰ These sections were analyzed for nanoindentation hardness properties along the metallic, calcium phosphate-coated, and calcium phosphate particulate (bone graft) interface regions with bone.

RESULTS AND DISCUSSION

History

From the perspective of a university-based program conducting retrieval and analysis studies, the worldwide networking for information and technique exchanges, consensus conferences, and consensus standards has been a valuable



Fig. 1. Midline nondecalcified thin section image of a plateau design root from implant retrieved after 60 months in vivo with a BIC of 52%.

asset. We believe that this approach will continue to benefit all stakeholders.

Conduct of Studies

The process for conducting and reporting of retrieval and analysis investigations has evolved significantly each decade. Currently, many programs exist throughout the world and the value of these types of analyses has been recognized by the profession. Going forward, this area is anticipated to expand as a component of assessing the quality, quantity, and longevity of health care based on surgical implant reconstructive procedures. One intent of the studies on outcomes from procedures using devices constructed from synthetic biomaterials has been to provide a platform of information for future combination and tissue regeneration procedures.

Examples of Dental Implant Studies

The three examples of dental implant studies summarized in this article have been published in part or submitted for journal publication. Therefore, data have been selected to present a brief overview of these types of results, and readers

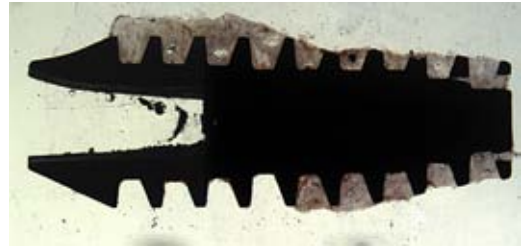


Fig. 2. Midline nondecalcified thin section image of a plateau design root form implant retrieved after 87 months in vivo with a BIC of 59%.

are referred to the references for more detailed information.

Example one: bone implant contact and histology for a root form dental implant

Examples of the bone, percent bone to implant contact (BIC) and appearance of midline longitudinal images from 5 and 7.25 years are shown in **Figs. 1** and **2**. This particular plateau design implant was constructed from titanium alloy and the surface treatments included (1) roughened by aluminum oxide particulate blasting, (2) plasma spray coating with unalloyed titanium particulate, and (3) calcium phosphate coating. Overall, the percent bone integration was similar for all surfaces (20%–80% BIC) for the 49 trephined specimens with in vivo times ranging from 6 months to 14 years.

Example two: Micro-CT analyses of bone grafts

An example of a midline micro-CT image from one of the 4 × 8 mm cylinder of bone trephined before dental implant placement is shown in **Fig. 3**.

Analyses permitted 3-D quantitation of the bone and bone graft dimensions. Overall, most of the original particulate graft of tricalcium phosphate had resorbed (>80%) during bone healing and the shape-related information showed that regional trabecular bone was progressing to structural maturity (from rods to plate geometry). As discussed in detail within the associated publication, these types of studies provided more quantitative

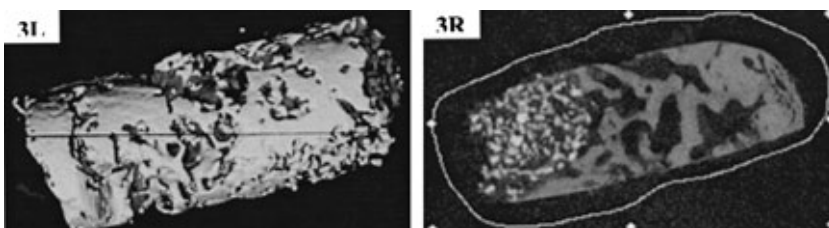


Fig. 3. Micro-CT image from midposition maxillary bone core implanted 12 weeks previously with a tricalcium phosphate bone graft substitute. Images 3L and 3R show 3D macro and 2D plane microscopic images respectively.

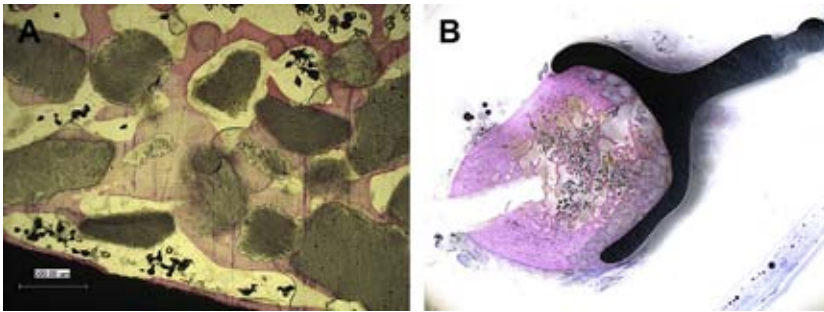


Fig. 4. Nondecalfied section of a postmortem 11-year mandibular implant with alloy and calcium phosphate particulate bone graft, microsection (*left*) and macrosection (*right*).

information compared with our former studies using histologic sections and histomorphometrical data.⁹

Example three: custom-coated implants with particulate grafts

Examples of nondecalfied thin sections prepared from a human donor mandible after approximately 11 years of implant function are shown in **Fig. 4**. Analyses of three similar donor specimens showed osseous integration of calcium phosphate coating, the alloy surface, and the calcium phosphate grafting particulates. These analyses support conditions of longer-term dental function for these types of constructs based on a significant magnitude of bone to implant integration (>30% of surfaces).

EXPERIENCE AND SUMMARY OPINIONS

An overall intent of this summary presentation has been to briefly explain the process of and provide examples from dental surgical implant device retrieval and analysis. Examples of study results have been summarized to demonstrate three areas where unique and new information has been or is being published within professional journals. An analysis of past and current activities strongly supports opportunities for more in-depth investigations of explanted (from revision) and postmortem (en bloc)-type specimens. The coordination of device and procedure registries with focused retrieval and analysis should continue to provide information to enhance clinical outcomes over the next decades. It seems that these types of protocols will be supportive of more fully investigating the clinical applications for successful and unsuccessful outcomes of evolving tissue-engineered medical products as alternatives to some types of synthetic-origin implant devices.

REFERENCES

1. Weinstein A, Gibbon D, Brown S, et al, editors. Implant retrieval: material and biological analysis. Washington, DC: U.S. Government Printing Office; 1981. p. 1–776. NBS Spec Pub. 601.
2. ASTM FO4-561-05, Am. Soc. Test. and Mat. Retrieval and analysis of medical devices and associated tissues and fluids, vol. 13.01. Conshohocken (PA): Annual Book of Standards, ASTM W; 2005. p. 136–51.
3. Retrieval and Analysis of Surgical Implants, ISO 12891-1,3. Geneva (Switzerland): International Organization for Standards; 2007.
4. Schnittman P, Shulman L, editors. Dental implants: benefit and risk, National Institute of Dental and Craniofacial Research/Public Health Service Pub No. 81–531, 1980.
5. Cochran D, Fritz M. Implant therapy I and II. *Ann Periodontol* 1996;1(1):707–821.
6. Conference Statement and Proceedings, NIH Technology Assessment Conference on improving implant performance through retrieval information: challenges and opportunities. Washington, DC: NIH; 2000.
7. Lemons J. Analyses of in situ and explant surgical implant devices, NIBIB-BRP Grant#R01EB001715, 2005–2010.
8. Lemons J, Anabtawi M, Beck P, et al. Retrieval and analysis of dental implants. *J Dent Res*, submitted for publication 2010.
9. Chopra P, Johnson M, Nagy T, et al. Microcomputed tomographic analysis of bone healing subsequent to graft placement. *J Biomed Mater Res B* 2009; 88B(2):611–8.
10. Baker MI, Eberhardt AW, McGwin G, et al. Bone properties surrounding hydroxyapatite-coated custom osseous integrated dental implants. *J Biomed Mater Res* 2010. Part B – JBMRB – 09–0574 [Accepted].