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# Histomorphometric evaluation of bone regeneration using bone substitutes materials on non-decalcified plastic-embedded specimens – a systematic review

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#### ADMINISTRATIVE INFORMATION

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**Review Stage at time of this submission -** Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

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**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 August 2024 and was last updated on 18 August 2024.

## INTRODUCTION

 $R^{\rm eview}$  question / Objective The purpose of this review is to establish which histomorphometric parameters assess the regeneration process using bone substitute materials on non-decalcified plastic-embedded specimens.

**Rationale** This review will examine which histomorphometric parameters are used in bone regeneration studies with bone replacement materials. Based on this research, clinicials will be able to determine which bone substitute to use in each individual case. Some situations require materials that are quickly resorbed, whereas others need longer times for the material to perform its osteoconductive function. Bone formation and material resorption rates will be evaluated with histomorphometric parameters. Histomorphometry is the gold standard for bone evaluation and the cellular level, as well as measuring bone metabolism and remodelling dynamics.

Condition being studied Bone regeneration using bone substitutes. This procedure is needed in cases of bone deficiency due to various reasons trauma, inflammation, malignancies etc. In our field of dentistry, bone deficiencies are most commonly caused by tooth loss and subsequent bone resorption. In order to adequately and predictably place dental implants, there should be sufficient bone volume in the edentulous site. In order to restore the required bone volume, bone augmentation is often performed, which is why this process is the focus of our study. We wish to determine which histomorphometric parameters are most commonly used and best describe the regeneration process, as well as which bone substitute materials perform best with regard to the forementioned parameters.

## METHODS

Search strategy Publications in English over the last 10 years (2015-2024). Databases: PubMed, Web of Science and SCOPUS. Terms: "histology",

"histomorphometry", "histomorphometric", "undecalcified", "non-decalcified", "bone substitute", "bone graft", "bone replacement material".

**Participant or population** This review will analyze animal studies in which bone regeneration is conducted, as well as human trials with patients undergoing bone regeneration, aumentation or preservation procedures, in which bone substitutes were used.

Intervention Procedures involving bone regeneration - bone augmentation, sinus floor augmentation, ridge preservation etc. In animal studies, often a critical size defect is created and filled with bone substitute materials, in order to simulate the bone deficiency conditions that require the abovementioned procedures. After a predetermined period of healing time, specimens from the regenerated area are obtained, embedded in plastic resin, stained with a dye and examined histomorphometrically. This examination includes various parameters such as the area of newly formed bone, residual graft material fraction and others. Our aim is to analyze which parameters other researchers use, how they assess the regeneration process and which bone substitutes perform best according to those parameters.

**Comparator** If applicable, controls with augmentation procedures with no bone substitute material will be included.

**Study designs to be included** Controlled animal studies; clinical trials and case series with at least 3 participants.

**Eligibility criteria** Inclusion criteria: full-text articles in English, published in the last 10 years (2015-2024), which fulfil the keywords in the search strategy.

Exclusion criteria: 1. review articles, books, book chapters, case reports and abstracts; 2. articles that do not discuss bone substitutes; 3. articles that do not discuss histomorphometric parameters or only mention semi-quantitative histomorphometric analysis; 4. articles that do not include plastic embedded specimens; 5. articles discussing decalcified specimens; 6. articles, in which histomorphometry is conducted with SEM; 7. articles discussing intraosseous implants.

**Information sources** The electronic databases Web of Science, Scopus and PubMed. **Main outcome(s)** Histomorphometric parameters which evaluate bone regeneration and their interpretation.

Additional outcome(s) Which bone substitute materials provide the best bone regeneration potential, based on histomorphometric parameters.

Quality assessment / Risk of bias analysis PRISMA guidlines for systematic reviews.

**Strategy of data synthesis** The titles, abstracts, author names, and years of publication of the studies will be exported to an MS Excel Spreadsheet. Then, duplicate records will be removed and the full-text studies were subjected to the inclusion and exclusion criteria. Screening will be conducted by two independent reviewers and discrepancies will be resolved through arbitration by a third reviewer. A tab will be created with all bone substitute materials used and the respective histomorphometric parameters. Afterwards, their significance will be discussed and evaluated. Qualitative assessment of study findings.

**Subgroup analysis** Based on the preliminary literature screening for our review, there are several animal models used in bone regeneration research. Many different biomaterials are being tested, with various healing times. This is why we intend to include subgroup analyses based on animal model, analysis time and bone substitute material.

Sensitivity analysis Not applicable.

Language restriction Articles only in English will be included.

Country(ies) involved Bulgaria.

**Keywords** histomorphometry; histomorphometric; bone substitute; bone graft; bone replacement material; bone regeneration; non-decalcified; plastic-embedded.

#### **Contributions of each author**

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