Numerical simulations on periprosthetic bone remodeling: a systematic review

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Abstract

Background and objective: The aim of the present study was to review the literature concerning the analysis of periprosthetic bone remodeling through finite element (FE) simulation.

Methods: A systematic review was conducted on 9 databases, taking into account a ten-year time period (from 2009 until 2020). The inclusion criteria were: articles published in English, publication date after 2009, full text articles, articles containing the keywords both in the abstract and in the title. The articles were classified through the following parameters: dimensionality of the simulation, modelling of the bone-prosthesis interface, output parameters, type of simulated prosthesis, bone remodeling algorithm.

Results: Sixty-seven articles were included in the study. Femur and tooth were the most evaluated bone segment (respectively 41.8% and 29.9%). The 55.2% of the evaluated articles used a bonded boneprosthesis interface, 73% used 3D simulations, 67.2% of the articles (45 articles) evaluate the bone remodeling by the bone density variation. At last, 59.7% of the articles employed algorithms based on a specific remodeling function.

Conclusions: Increasing interest in the bone remodeling FE analysis in different bone segments emerged from the review, and heterogeneous solutions were adopted. An optimal balance between computational cost and accuracy is needed to accurately simulate the bone remodeling phenomenon in the postoperative period.

1. Introduction

Bone remodeling is a widely studied topic within the framework of the human body physiology. It is a cyclic and continuous process that involves the bone in its structural adaptation to external mechanical stresses [1]. Therefore, each subject's experiences concur to specific bone biomechanical adaptation. After the insertion of a foreign body, e.g. a prosthetic implant, the bone tissues undergo substantial bone structure and density changes that might lead, over time, to the total osseointegration [2]. Indeed, the primary and secondary stability must be achieved to guarantee the success of a prosthetic implant [3]. The evaluation of such changes is therefore crucial to assess the quality of an intervention, as well as the risk of implant mobilization and failure.

The densitometry is a well-established quantitative method to evaluate bone remodeling [4]. Nonetheless, densitometry is not a predictive analysis, and it gives no possibilities to evaluate outcomes coming from specific biomechanical conditions. Finite element (FE) simulations could instead offer interesting insights regarding the bone remodeling in prosthetic implant scenarios [5]. Given the increasing computational and clinical power of FE analyses, an extensive comprehension of the recent state of art on bone remodeling results crucial to understand how mechanical aspects have been translated into biological inferences. Although several studies assessed the bone remodeling phenomenon through numerical simulations, no literature reviews have been conducted to give a comprehensive overview of the current approaches.

Thus, the aim of the present study was to systematically review the current literature concerning the analysis of periprosthetic bone remodeling through FE simulation. The present systematic review meant to give an overview of the main features adopted in numerical studies regarding the bone remodeling phenomenon in the last decade.

2. Materials and methods

2.1. Literature research

This systematic review has been conducted following the PRISMA Statement checklist [6].

A literature search was conducted on 9 different databases: PubMed, Biomedcentral, Cochrane, Web of science, Pedro, IEEE, Wiley, Science direct, and SpringerLink. The query string that has been used for the research was "(bone remodeling) AND (Finite Element (model OR method OR analysis)) AND ((Osseointegration) OR(Osteointegration) OR (Bone ingrowth)).

2.2. Inclusion and exclusion criteria

The inclusion criteria were:

- Language: English
- Time: publication date after 2009
- Full text articles
- Articles containing the keywords both in the abstract and in the title

The exclusion criteria were:

- Language: Articles written in other languages except in English
- Time: date prior to 2009
- Case report studies
- Clinical trials and follow-ups.
- Review articles
- Metanalysis

2.3. Quality assessment

The quality of the included study was assessed through the Quality Assessment model proposed by Salimi et al. [7]. For the purpose of the present study, this model was customized by using citation metrics and scientific collaboration metrics. These two metrics are summarized by two indicators, Journal Impact Factor (JIF) and Scimago Journal Rank (SJR). Both indicators published in the year of publication of the article were used. We included the articles with JIF>1 and journals that are part of quartiles Q1 and Q2 proposed by SJR.

2.4. Studies selection

In the last 10 years, 783 articles emerged from the review (Fig. 1). From the previous selection, 72 were published in multiple journals, so they were considered only once (from the first journal they were found in) for the purposes of final counting. Through the reading of the abstract, 255 were excluded because not relevant with the search carried out. The total relevant articles were 456. From this moment on, all the articles have been read in their entirety. Initially, articles that did not contain finite element simulations were excluded, and the number decreased to 328. The more clean-cut occurred through the exclusion of articles that do not present an algorithm of bone remodeling in the FEM simulation. Therefore, all those articles that simulate exclusively the interaction or the effort to the interface bone-prosthesis, without evaluating the morphological changes of bone (e.g. bone density variation), have been excluded from the research. At the end, 18 articles were excluded after application of quality assessment indicators.

After this last step, the final articles that have been included are 67 in total. Two authors (A.M., S.P.) independently reviewed each article's title and abstract from the literature search. The assessors were not blinded to the authors of the publications. The full text was obtained and evaluated when eligibility could not be assessed from the first screening. Any disagreements were resolved via a consensus discussion between the reviewers, and a third reviewer (S.D.P.) was consulted if the disagreement could not be resolved.

3. Results

From the 783 initial articles, a total of 67 articles were included in the qualitative summary. About 95% of the articles are published on Science Direct, Pubmed and Springer Links (24, 26 and 12 articles respectively). Four articles were found on IEEE, and one article was found on Web of Science. None of the selected article was retrieved on Biomedcentral, Wiley, Cochrane and Pedro databases.

The average of JIF was 3.01, the average SJR was 1.16, 65% of articles were from Q1. The quality indicators of each study are listed in Appendix A. The articles were classified by:

- Simulated bone segment (e.g., femur, tibia, tooth, etc.)
- Bone-Implant interface (boundary condition for the interaction between bone and prosthetic implant)
- Dimensionality of the simulation (e.g., 2D or 3D)
- Bone remodeling algorithm (algorithm used to simulate the bone remodeling phenomenon)
- Output parameters (output of each numerical simulation) See the Appendix B for the full article list.

3.1. Bone segment

The FE simulations were mainly conducted on specific bone segments and implants (Fig. 2). Of the sixty-seven articles included in the review, ten articles related to generic tissue [8–17], while four articles simulated tibia bone in animals (three about rat's bone [18–20] and one about rabbit's bone [21]).

Fifty-three articles related to human bone segment. Of these, twenty-eight articles simulated the femur [22–49], twenty the tooth [50–69], two humerus [70,71], and one the tibia [72], the glenoid [73], and the pelvis [74] .

3.2. *Bone-implant interface*

The modeling of bone-implant interaction was heterogeneous in the retrieved studies (Fig. 3). The majority used a bonded interface [15,16,18–20,24–31,33,35,36,38,41,44,47–50,53,55–57,60–62,64–68,72,73] (Fig. 3), i.e. the surfaces of the two bodies remain in contact during the simulation in order to avoid relative rotations and translations. In this case, the bonded interface constituted a zone with no friction. When a friction zone was inserted, a coefficient of viscous friction ranging from 0.4 to 0.5 was used [17,22,23,32,34–37,39,42,43,58,59,68,70,71,73,74].

Fig. 4.

Another approach consisted in inserting a layer of soft tissue to simulate the bone growth (osteogenesis) and the subsequent formation of mature bone [10,11,13,14,21,46,54,63]. The latter approach allows to evaluate the stress and strain of the newly formed bone.

Moreover, two studies simulated a layer of blood between the implant and the bone [52,69] in order to account for the first postoperative phase. This way, the extent of the preload and the time elapsed between the operation and the first mechanical solicitation of the prosthetic body portion could be evaluated.

Two more studies simulated cemented implants by inserting a layer of polymeric material between the bone and the prosthesis [31,40]. This layer fills the micropores of the bone tissue, influencing the load distribution and bone remodeling outcomes.

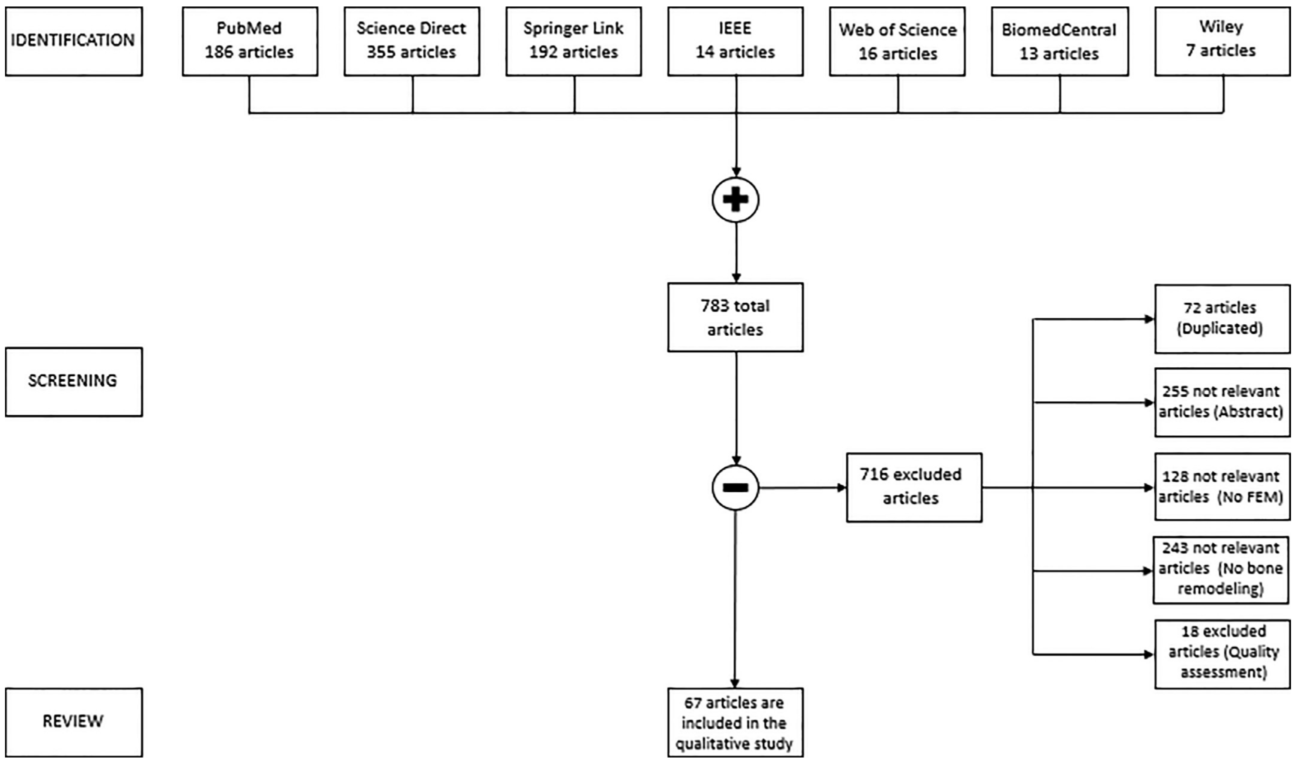

Fig. 1. Flow diagram of research process.

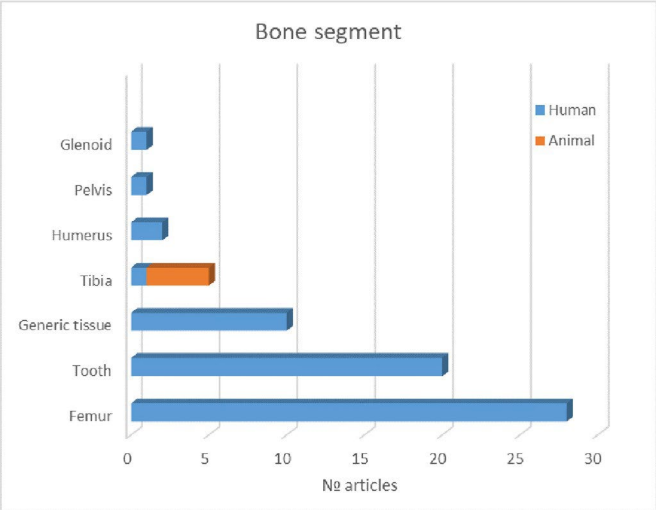

Fig. 2. Articles concerning specific human bone segment

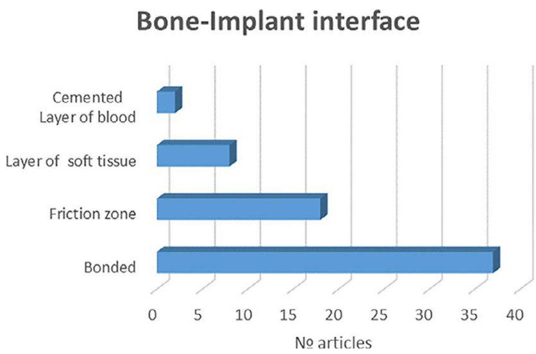

Fig. 3. Articles concerning bone-implant interface.

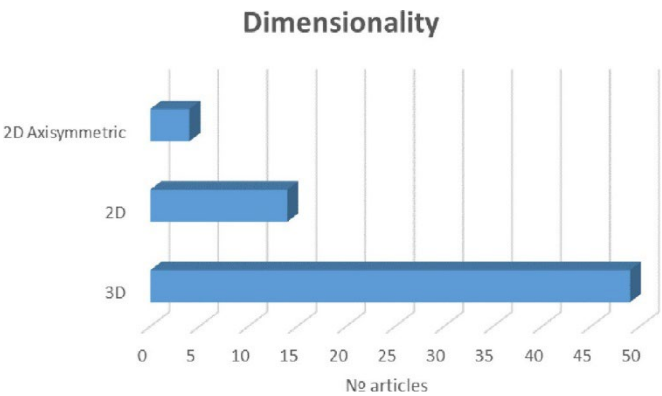

Fig. 4. Articles concerning dimensionality of modeling

3.3. Dimensionality of modeling

The most of the evaluated studies (73%) use 3D simulations [9,15,17–27,29–42,44,46–51,53,55,56,60–62,64–68,70–74].

Of the remaining 27% of the articles, 21.1% use 2D simulations [8,10–12,14,28,43,45,52,54,57–59,69] and 5.9% use 2D axisymmetric simulations (4 articles [13,16,21,63]).

A total of 21 different bone remodeling algorithms were retrieved (Fig. 5A). The main differences between the algorithms regarded the complexity of bone apposition/deposition simulation. The most used algorithm (25 studies, 37.3%) is the one proposed by Huiskes and Weinans [75] in 1987. On the basis of this function, 15 other studies modified the original version to adapt it to their studies [76–79]. Either the original or the adapted algorithm was used in 40 of 67 articles (59.7%).

Other algorithms were used only in up to 6 (Li et al. [76]), 4 (Stanford theory [79] and Doblare et al.[80]), or less studies. Each algorithm evaluated changes in bone density through one of the following parameters:

- Interface displacement [10,12,81,82];
- Stress or deformation tensor [83,84],[80,85,86];

- Bone affixing/deposition rate [87];
- Activation of osteoblasts and osteoclasts [9];
- Distinction between fibrous, cartilage and mature bone growth [88,89];
- Meshless method [90];
- Stochastic gradient descent to optimize the results obtained [91];
- Studies of 3 macro levels such as bone remodeling, interface displacement and level of osteointegration [15].

In 9 articles, the Young modulus of the investigated bone segment was iteratively updated through the bone density formulation of Taylor et al. [92], while 9 articles used the formulation of Keaveny et al [93] .

Output parameters differed among the studies (Fig. 5B). About 70% of the studies evaluated the bone density changes during the bone remodeling process [9,13,15– 17,19,20,22–29,31,32,34,37–43,45,47–53,56,58–61,66,69–74].

Other outcomes were: micromovements at the interface [21,22,24,31,33–35,39,42,48,50,53,58,59,62–64,68,71], the stress distribution on the bone or implant [15,22,27,30,31,34-36,44,45,47,49,55,57,62,64–66], the strain distribution [18,20,29–31,33–35,40,44,45,50,62,67,68,73,74].

4. Discussion

The present systematic review aimed to analyze the characteristics of FE simulations on periprosthetic bone remodeling phenomenon. The most important findings of the present study were:

- Femur and tooth were the most investigated bone segment
- A bonded bone-implant interface was used in about half of the studies
- 3D simulations were predominantly used
- The bone remodeling function proposed by Huiskes et al. [1] was used in more than half of the retrieved studies
- The change in bone density was the most investigated output parameter

Based on these findings, it was possible to clarify the current use of FE simulations to investigate the bone remodeling. Although many studies had similar focuses, heterogeneous approaches were used for the different parameters.

Increasing interest in the FE simulation of bone remodeling emerged from the review. Dental and hip implants were the most investigated. Such implants are likely to fail because of bone resorption and subsequent mobilization, while other bone segments’ implants do not usually undergo the same relative loadings. However, the focus on bone segments has been changing over the decade. Indeed, the latter were mostly retrieved from 2009 to 2012, while osseointegrated transfemoral and transtibial or shoulder prostheses were investigated in the last five years [94,95]. Such surgical approaches are relatively new [96] and might need a specific analysis of bone remodeling due to their particular loading conditions.

Regarding the bone-implant interface, a bonded solution represents a coarse approximation. Indeed, it is used to simulate a complete osseointegration when relative micromovements are no longer present. Nevertheless, this is likely to occur after a long period from surgery or in static loading condition. A viscous interface is a minimum requirement, e.g., in simulations of joints with a wide range of motion, such as hip and shoulder. Different approaches in which layers of soft tissues are inserted might allow to better estimate the stress and strain of the newly formed bone, thus getting closer to a plausible early bone remodeling phenomenon.

The FE simulations usually adopt 3D models since the prosthetic implants do not comply with symmetry conditions. When the axial-symmetric condition occurs, 3D models can be approximated to 2D ones, such as in orthopedic screw or a dental implant. This approximation allows to reduce the modeling computational cost and use a more exhaustive algorithm.

Indeed, the bone remodeling function described by Huiskes et al. [75] has a low computational cost, is ductile and can be easily adapted to different scenarios and applies indiscriminately to all the bone segments. For these reasons, it remained the mostly used even if it was implemented more than four decades ago. This algorithm would therefore represent a gold standard for bone remodeling FE simulations, although its applicability should be accurately validated for clinical support use. Iterative formulations to update the Young modulus according to the bone density changes [92,93] were used in one third of the articles. Such formulations could be relevant for numerical simulations of bone remodeling in wide time ranges.

The most used output parameter used to evaluate the bone remodeling was the change in bone density. It allows both to simulate the stability condition of the prosthetic implant and validate the FE model against experimental tests like the bone densitometry. It must be underlined that, from a mechanochemical point of view, the correct cause/effect relation in the bone remodeling phenomenon is not always respected in the presented algorithms. Indeed, some output parameters (e.g., stress/strain distribution) should instead be considered as input features of the bone remodeling.

Different uses of the numerical simulations could be evidenced in the present review. The most used approach (half of the retrieved articles) was the description of the bone remodeling phenomenon; one-third of the articles aimed to predict the phenomenon, while about the 20% aimed to explain it (Appendix B). In the authors' opinion, the predictive approach could be the most supportive in the clinical assessment of periprosthetic bone remodeling.

The present study has some limitations. Among the 21 algorithms retrieved, 10 were not validated by experimental results. Other 7 algorithms were only confirmed by the results emerged from other studies. Only 4 algorithms, used in 7 studies, were validated through densitometry. The need for validated algorithms is a key point to endorse the use of FE simulations of bone remodeling in daily clinical practice. Furthermore, no studies reported information regarding the stability/convergence problems of the algorithms used and few studies reported the time range of the numerical simulation. Regarding the latter point, the time range simulated was highly heterogeneous among the different studies. Another limitation regards the articles' quality assessment. Since no specific quality assessment tool has been designed for studies regarding FE simulations, the most similar solution [7] was partially customized for the purpose of the present study.

The present systematic review underlined the mostly used features of numerical simulations investigating bone remodeling phenomenon. No single optimal approach can be determined, and the different features should be chosen with respect to the specific investigation. For example, the choice of the bone-implant interface is strongly connected to the density of the bone (trabecular or cortical) under investigation and to the biological timing of the bone formation (immediate postoperative, late postoperative). Future numerical simulations should achieve the goal of predicting the bone remodeling during the planning of the surgery through a patient-specific approach. The latter aspect might boost the clinical power of such numerical simulations. An optimal solution should predict the bone remodeling phenomenon as accurately as possible in each different case without escalating the computational cost of the numerical simulation.

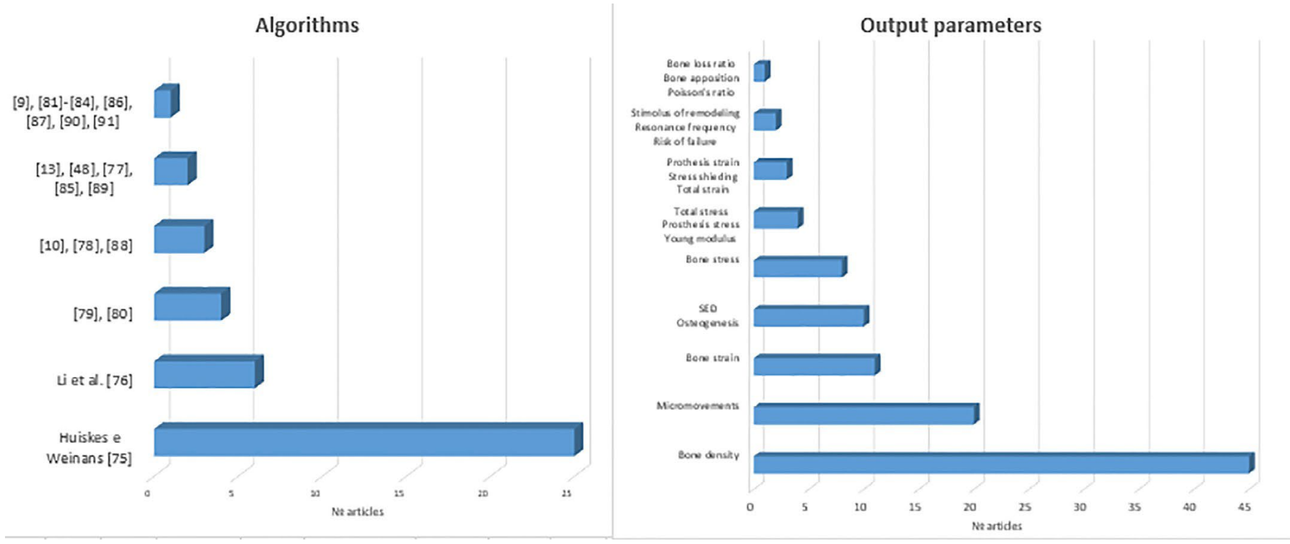

Fig. 5. Left) Articles concerning algorithm of bone remodeling. Right) Articles concerning output parameters.

5. Conclusions

Heterogeneous solutions were adopted either regarding the algorithms, the bone-implant interfaces or the output parameters. An optimal balance between computational cost and accuracy is needed to accurately simulate the bone remodeling phenomenon, with specific modeling parameters for the different bone segments and post-operative periods.

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Declaration of Competing Interest

The authors declare that there is no conflict of interests regarding the publication of this article.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cmpb.2021.106072.

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