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Influence of growth plate morphology on bone trabecular groups, a framework computational approach

Diego Quexada-Rodríguez [a,b], Olfa Trabelsi [a], Marie-Christine Hobatho [a], Salah Ramtani [c], Diego Garzón-Alvarado [b,*]

[a] Université de Technologie de Compiègne, CNRS, Biomechanics and Bioengineering, Centre de Recherche Royallieu, CS 60 319 - 60 203 Compiègne Cedex, France
[b] Numerical Methods and Modeling Research Group (GNUM), Universidad Nacional de Colombia, Colombia
[c] Université Sorbonne Paris Nord, Laboratoire CSPBAT, équipe LBPS, CNRS (UMR 7244), Institut Galilée, F93430 Villetaneuse, France

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ABSTRACT

The morphology of the growth plate undergoes various transformations during each stage of development, affecting its shape, width, density, and other characteristics. This significantly impacts the distribution of stress in the epiphysis of long bones. To the best of our knowledge, this study represents the first attempt to examine the relationship between growth plate morphology and trabecular bone patterns. Our analysis was conducted using a finite element model and we analyzed two medical cases: trabecular patterns in the femoral epiphysis and the calcaneus bone. Our findings revealed a correlation between the formation of main trabecular groups and growth plate morphology. We investigated how an increased density in high-shear stress zones, which are typically located at the periphery of the growth plate, may occur to prevent failure by shear. This is evident in cases such as slipped capital femoral epiphysis or sever's disease, different simulations align with the clinical data available in the literature from a qualitative and quantitative point of view. Our results suggest that further research should focus on understanding the impact of growth plate morphology on bone remodeling and exploring potential preventive measures for different bone disorders.

1. Introduction

Development of long bones takes place mainly in the growth plate or epiphyseal plate, this zone is composed mainly by hyalin cartilage which is composed of approximately 70 % water and a solid matrix formed mainly by collagen type II [1] and is used as a mold or template at both ends of each bone where a primary ossification center is formed. The growth plate is divided into three main zones: Reserve zone, proliferating zone, and hypertrophic zone. Each layer has been found to exhibit different mechanical properties this is mostly due to their different extracellular composition and grade of mineralization, the proliferative zone stands out for being the highest in proteoglycan content which gives it an incompressible behavior, the hypertrophic zone has a high degree of calcified matrix so it has a more rigid behavior [2].

There are different theories that relate the mechanical state of the growth plate with its development, among the featured models the one by Carter and Wong [3] relates cartilage formation with octahedral normal stress while spongy bone is formed due to shear stresses, with this two stresses they defined the osteogenic index (OI) which has been used extensively in the modeling of cartilage and bone formation in joints and different ossification centers [4].

During postnatal growth, bone remodeling plays a major role in defining the topology of the internal bone structure in addition to endochondral growth, that is the process directly responsible for longitudinal growth in long bones. Regarding the bone remodeling process which accounts for a dynamic in which formation and resorption are dependent one another, there are various modeling approaches that consider the different mechanical and biological factors that influence this process. There are five phases conforming the bone remodeling process: activation, resorption, reversal, formation, and quiescence. These processes occur continually and are key in understanding bone remodeling. Most relevant models found in the literature address partially or totally each one of these phases. One of the first models to relate the state of mechanical load to bone remodeling was that of Wolff

Abbreviations: OI, Osteogenic index; BMU, Bone multicellular unit; UEL, User-defined elements; PTG, Principal tension groups; SCG, Secondary compression groups; FEM, Finite element method.

* Corresponding author.
E-mail address: dagarzona@unal.edu.co (D. Garzón-Alvarado).

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et al. published in 1807. Wolff's law states that bone remodeling occurs in response to change in the stress distribution in bone, in functioning remodeling this response, it reorients the trabeculae so they have a topology determined by the stress field, corresponding with principal stress trajectories. This research established the foundations of the mechanics of modern bone remodeling, allowing for deeper research on how calcium homeostasis works, how local micro-damage repair occurs and which biological factors are most important in this process [5]. During the mid-20th century, several cell population models were developed, among which the one by Lemaire et al. [6] relates the activation of osteoblasts and osteoclasts in dependence on the RANK-RANKL-OPG signaling pathway and uses the mature and immature portion of the osteoblast population to control the degree of osteoclast activity. Geris et al. [7] proposed a model using partial differential equations to describe bone formation using a time-space scheme that varies according to cell densities and concentrations of growth factors. Postulated a growth factor diffusion model and ordinary differential equations to describe signaling pathways and agents that simulate the action of various cell types involved in vascularized bone regeneration within a CaP scaffold loaded with growth factors. Another important mathematical model is that of Komarova et al. [8]. who proposed a set of population differential equations of osteoclasts, osteoblasts, and mutually regulating factors that adequately represent the biophysical process with the existence of periodic solutions, which correlate with the phases of activation and resorption. Among the featured models, that of Weinans et al. [9], is based on strain energy as the main determinant of localized bone density in trabecular structures and proposes a set of bone remodeling differential equations, integrated with the finite element method using 2D elements, where the solution obtained resembles the density distribution of bone, showing the formation of the main trabecular groups.

The morphology of growth plates and bone remodeling are closely related and both are affected by mechanical stimuli. Therefore, this study aims to investigate the influence of growth plate morphology on trabecular patterns in long bones. This model could potentially be applied to pathologies such as slipped capital femoral head, Osgood-Schlatte, or Sever's disease that affect both the growth plate and trabecular formations. Using the bone remodeling response model proposed by [10], we will analyze trabecular patterns in the epiphysis of the femur and the calcaneus bone. Our findings will shed light on the correlation between growth plate morphology and trabecular patterns in these pathological conditions, which could help us understand their onset and progression. Ultimately, this could lead to the development of new preventative strategies.

2. Methods

In this section, the numerical approach to solve the bone remodeling problem, with a linear isotropic behavior, and the benchmark tests will be presented.

2.1. Model description

The remodeling algorithm seen in Fig. 1, uses the strain energy per unit of volume as the main stimuli for bone remodeling, and is based on the work by Garzón-Alvarado and Linero [11] and Nackenhorst [10], where Eq. (1) states that the gradient of the stresses field σ is in equilibrium with body forces b. This equation is coupled with the evolution law stated in Eq. (2), here the dimensionless density λ depends on the strain energy per unit volume U at the finite element, and a strain energy U_{ref} which sets the threshold for bone formation or resorption, k_1 is the constant of remodeling speed and n is an exponent found experimentally. To calculate U in (Eq. (3)), the strain energy density $W(\rho)$ is first estimated as a function of bone density ρ, $W(\rho)$ depends on the strain vector ε and the stiffness matrix C_0 as seen in Eq. (4). In each time step the elastic modulus E_0 is updated following a power law as stated in Eq. (5).

$$\nabla^T \sigma + b = 0 \tag{1}$$

$$\frac{d\lambda}{dt} = k_1 \left[\lambda^{n-1} \frac{U_{str}}{U_{ref}} - 1 \right] \tag{2}$$

$$U = \rho_0 W(\rho) \tag{3}$$

$$W(\rho) = \frac{1}{2\rho} \lambda^n \varepsilon^T C_0 \varepsilon = \frac{\lambda^n}{\rho} \left[\frac{\varepsilon^T C_0 \varepsilon}{2} \right] = \frac{\lambda^n}{\rho} U_{str} \tag{4}$$

As a convergence criterion for the algorithm, the stop condition was set to 100 days with a timestep of 0.1 days, since density shows negligible changes after this moment. This goes in accordance to the findings

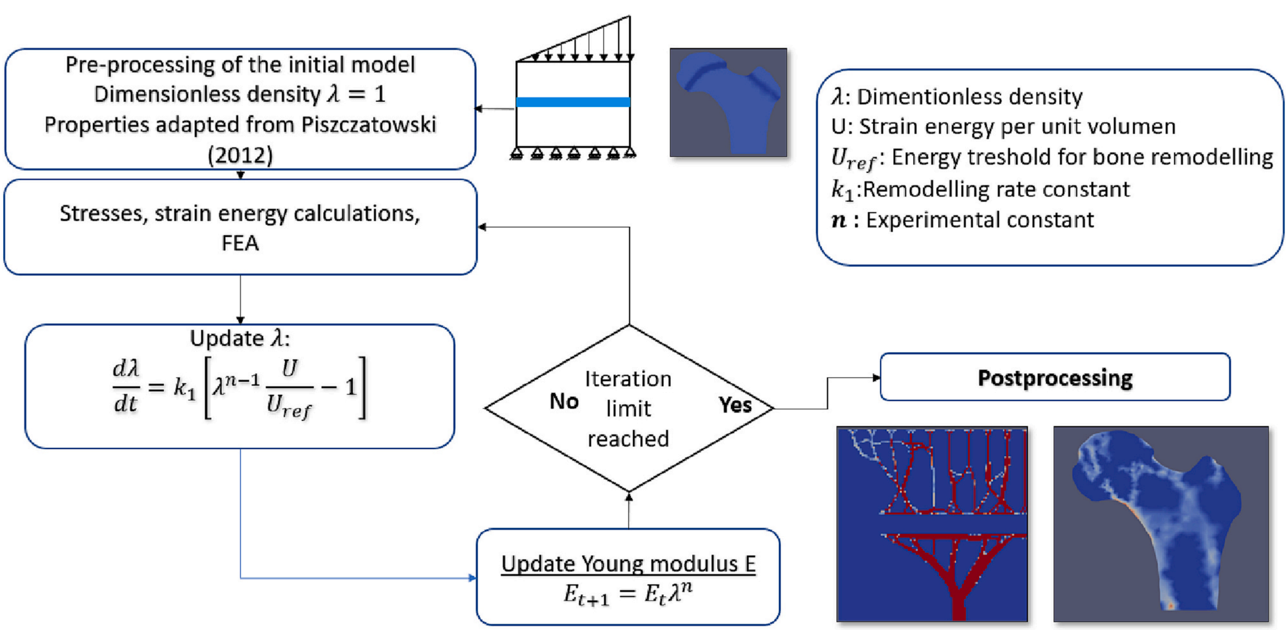

Fig. 1. Bone remodeling algorithm.

of Buenzli et al. [12] for the quasi-steady state found at this time for the cell population of osteoblasts and osteoclasts in the bone multicellular units (BMU), other works have used the same steady state time [11].

In the medical cases, for the femur, the boundary conditions proposed by Beaupre and Orr [13] were implemented, this accounts for a loading history where the hip reaction force and the abductor muscle are mostly present while the gait cycle is taking place. Whereas in the calcaneus case, the boundary conditions account for the loading during gait, particularly for the lifting movement of the foot, as proposed by Belinha et al. [14].

$$E(\lambda) = E_0\lambda^n \tag{5}$$

2.2. Numerical implementation

The bone remodeling problem was solved using a user element defined subroutine (UEL, ABAQUS 2017). An integration scheme of Runge Kutta 4th order was utilized for the evolution law. The FEM simulations were 2D cases that considered plane stress and were addressed using triangular and quadrilateral linear elements. A convergence analysis was carried out for each mesh, with an allowable change of no higher than 5 % in stress, which is one of the main mechanical stimuli responsible for bone remodeling, used as the refinement criteria. The benchmark tests employed a characteristic length of 1 mm, while the medical cases for the femur and calcaneus used 0.1 mm and 0.05 mm, respectively. In all cases, convergence was verified to ensure that the resultant topologies were independent of the mesh used.

To begin, we tested various scenarios on a benchmark domain to evaluate the bone remodeling scheme, as discussed in previous studies by Garzón-Alvarado and Linero [11]) and Nackenhorst [10].This time, we considered the presence of the growth plate and its influence on bone remodeling. To define the mechanical properties, we referred to the works of Piszczatowski [2] and Piszczatowski [15] for trabecular bone, and we averaged the properties at the different layers of the cartilaginous growth plate, as reported by Gao et al. [16]. Furthermore, we adopted all constants for the evolution law in Eq. (2) and Eq. (6) from Garzón-Alvarado and Linero [11] previous work (2012b).

Fig. 2 displays an epiphyseal scar, which is the region where endochondral ossification occurred. When the entire domain was left to undergo the bone remodeling process for an arbitrary time, a continuous columnar structure was observed towards the supports after the mineralization of the growth plate, as depicted in blue in Fig. 2.

Fig. 3 illustrates the formation of uniform, plate-like structures at the interface of cartilage and trabecular bone. As we will discuss in the following sections, this phenomenon results from a uniform stress field in the growth plate's vicinity. We also tested various locations for the growth plate, and the outcomes indicate an increase in bone columnar formations when the growth plate is situated closer to the boundary conditions.

3. Results

The results of both femur and calcaneus bones have revealed the presence of trabecular groups, with the most prominent being the principal tension groups (PTG) and secondary compression groups (SCG) [17], as depicted in Figs. 4 and 5. Other markers, such as Ward's triangle can be identified in Fig. 4. In all simulations, a separation corresponding to the epiphyseal plate is noticeable, but the pattern extends beyond this point, particularly for the compression groups. The calcaneus bone exhibits the most visible thalamic group in Fig. 6. In addition, an increase in bone density is observed in the peripheral areas where shear stresses are higher, particularly in growth plates with a convex shape.

Fig. 5 illustrates how the shape of the growth plate affects the bone remodeling process. Notably, the most significant change occurs in the principal tension group, where an increase in density is observed due to the convex shape. This effect becomes more pronounced in the final stages of development.

4. Discussion

Growth plate morphology has an influence on stress field distribution in long bones, especially in the epiphysis, as stated by Guevara et al. [18]. This in turn has a direct consequence on the trabecular bone patterns as can be seen in the results. Relevant features such as Ward's triangle can be identified, besides the main trabecular groups in two of the principal trabecular bones in the human body, the femur and the calcaneus.

As seen in Fig. 6, there is an increase in bone density in the areas nearby the peripherical part of the growth plate, this can be seen

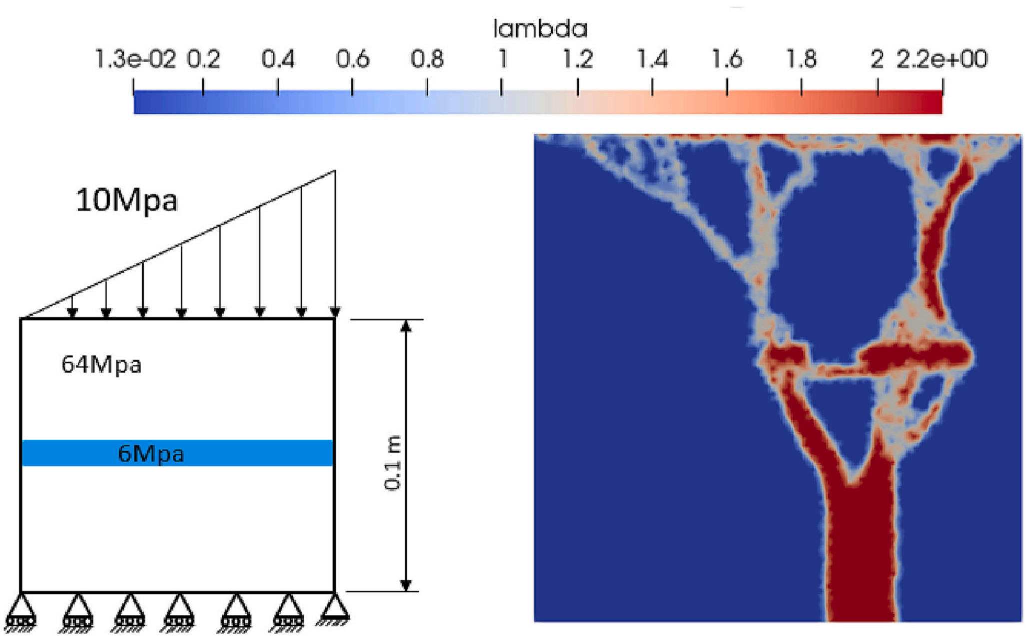

Fig. 2. Benchmark test, boundary conditions and results showing topology with epiphyseal scar.

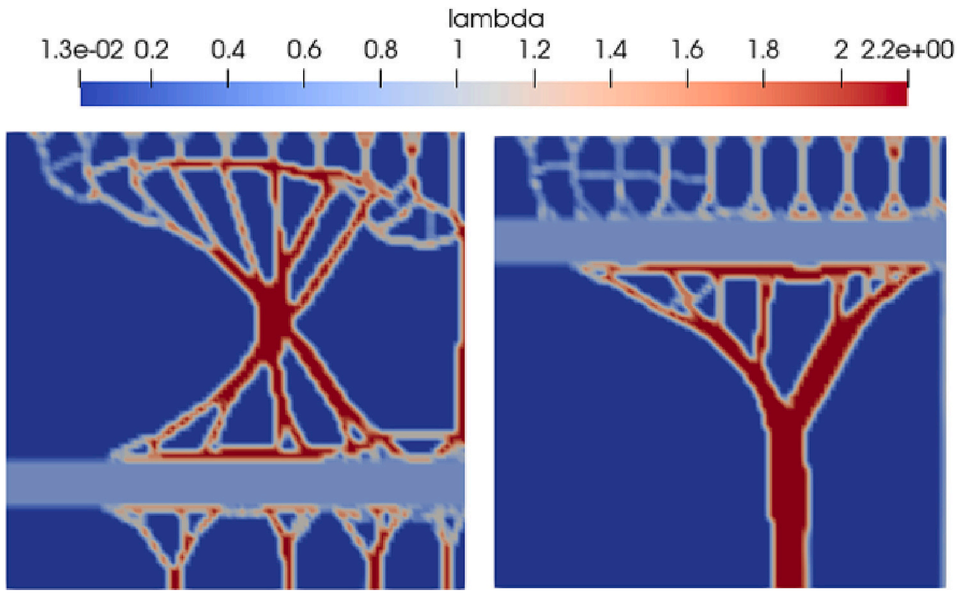

Fig. 3. Benchmark test where altering the vertical position of the growth plate within the domain produces varying trabecular formations.

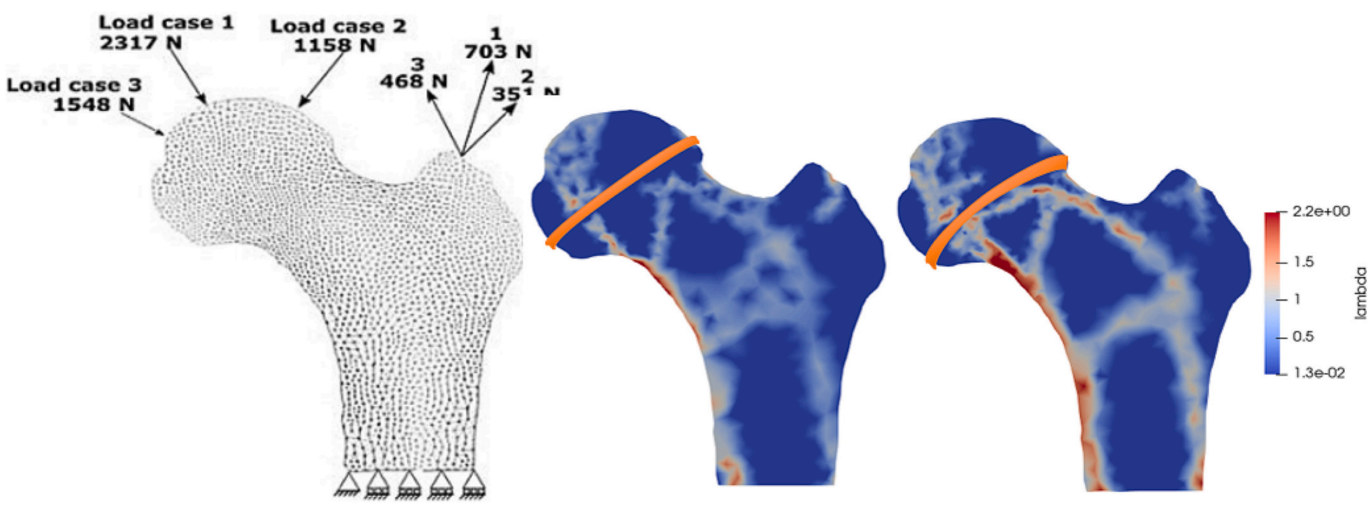

Fig. 4. Boundary conditions and main trabecular groups, for a planar and convex growth plate.

specially in the case of the convex shape. The results showing an increased bone density in high shear stress locations go in agreement with the findings of Staines et al. [19] who studied the bridge formation within the epiphyseal plate using μCT scans and found an increased density in the peripheric area of the growth plate where the shear stresses are higher. In the simulations, trabecular groups have been identified as bone with high percentage of trabecular mass. This change is hypothesized to serve as an adaptation in zones prone to failure by shear. For the femur, the most visible groups are the PTG and the SCG, which delimitate Ward's triangle. Changes in the compression groups density are seen especially in the peripherical part of the epiphyseal plate when a convex shape is formed (similar at topologies found at 10 years old), which agrees with the hypothesis given by Kandzierski et al. [20]. A similar behavior can be seen for the calcaneus bone, in which change in density may prevent some pathologies like Sever's disease in which repetitive shear stress can affect the apophysis, and produce segmentation of the calcaneal apophysis.

The wavy pattern, which is typical in the late stages of bone development (after 7 years old), could arise from the variation of trabecular patterns that distribute the load in a non-uniform manner in the growth plate. Furthermore, the increased density near the growth plate, marked in red in Fig. 5, is associated with sharp curves in the growth plate that act as stress concentrators, especially for the deviatoric stresses (Fig. 7).

In the calcaneus, main trabecular groups are obtained with an increased density near the Achilles tendon, which is a critical zone as it is submitted to high shear stresses [21]. The results show how a bone remodeling scheme is affected by changes in growth plate topology. Additional models adding the cartilaginous mechanical behavior can be implemented to see how the growth plate changes over time according to the load perceived by the main trabecular groups in a localized manner, this approach may be addressed in a future work.

It is important to note that the findings of this study should be interpreted with caution due to certain limitations. Firstly, the study only examined two medical cases, which may not be indicative of the patient-specific geometry. Secondly, the study employed a linear model to analyze the bone remodeling response. This model assumes that the bone adapts in a linear fashion to changes in mechanical load that are considered stationary, representing an average of the normal loading conditions. However, in reality, bone adaptation occurs through the influence of different cyclic forces [22] and that are often related to

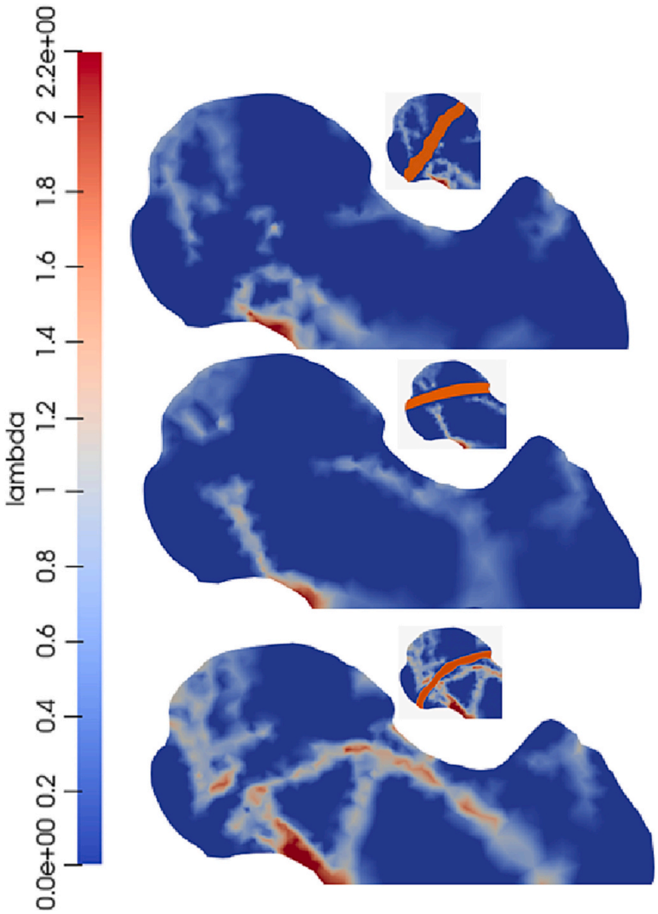

Fig. 5. Growth plate shape affecting bone remodeling.

damage which is considered an important stimulus in bone remodeling. To address this, previous researchers have adopted an approach that averages the loading conditions such as Nackenhorst [10] and Belinha et al. [14].

While this model has been widely used in the literature, it may not fully capture the complexity of bone adaptation in vivo. Furthermore, the study did not consider anisotropy in the bone structure, only local material properties changes in each element due to the bone remodeling scheme updating each element young modulus. Considering an anisotropic model in the formulation, is an important aspect to consider in future studies as it would give a more accurate representation of the bone microstructure. Nonetheless, the use of linearity in the bone remodeling model is justified as it allows for simple and computationally efficient analysis, as previously proposed by Carter and Wong [23] and Gao et al. [24].

5. Conclusions

This work shows how the growth plate shape may affect the self-enhancing process in which a high strain energy density area may result in denser bone at each timestep. The trabecular patterns that emerge as a result of this process give information on the stress field that is affected by the growth plate presence and shape. Furthermore, the epiphyseal plate is found to act as a uniformizer of the stress fields and in consequence the main trabecular patterns.

This pattern formation results of interest in pathological cases affecting the growth plate since the load transmission to the growth plate may be localized in different areas, which will determine the mechanobiological response of the growth plate. This may be of special interest in the recovery of salter Harris fractures, or in the treatment of slipped capital femoral head where transphiseal screws have been used in adolescents to prevent further slippage and collapse, and to improve density in certain areas subjected to high shear stresses [25]. From the benchmark tests and the medical cases simulations, it is seen the formation of uniform plate like structures that may transfer load in a more uniform way and may be directly responsible for the change in shape of the growth plate during different developmental stages.

As a future work and to go further into the mechanobiology of the growth plate, the exact mechanisms in which the growth plate is affected by the action of the trabecular patterns may be studied using a bone remodeling dynamic. Since the trabecular patterns seem to have an important role in the change of shape in the growth plate, a scheme were the changes in shape are due to direct influence of the trabecular pattern seems like a promising research path. Also, models adding the cartilaginous mechanical behavior can be implemented to see how the growth plate changes over time according to the load perceived by the main trabecular groups.

CRediT authorship contribution statement

The study was collaboratively designed by all authors as part of a cotutelle Ph.D. program between the Universidad Nacional de Colombia and the Université de Technologie de Compiègne. The first author, Diego Alfredo Quexada Rodríguez, drafted the manuscript, with the assistance of Professors Olfa Trabelsi and Diego Garzón, who provided valuable corrections. Professors Marie-Christine Ho-Ba-Tho and Salah Ramtani played a crucial role in conceiving the study and providing insightful guidance.

Declaration of competing interest

We, the authors of the manuscript submitted to your esteemed journal, would like to confirm that there are no conflicts of interest to declare. Our study was conducted with integrity and objectivity, and we have no financial or personal relationships that may have influenced the results or interpretation of our findings. We believe that our research is important and valuable to the scientific community and we are committed to upholding the highest standards of ethics in our work.

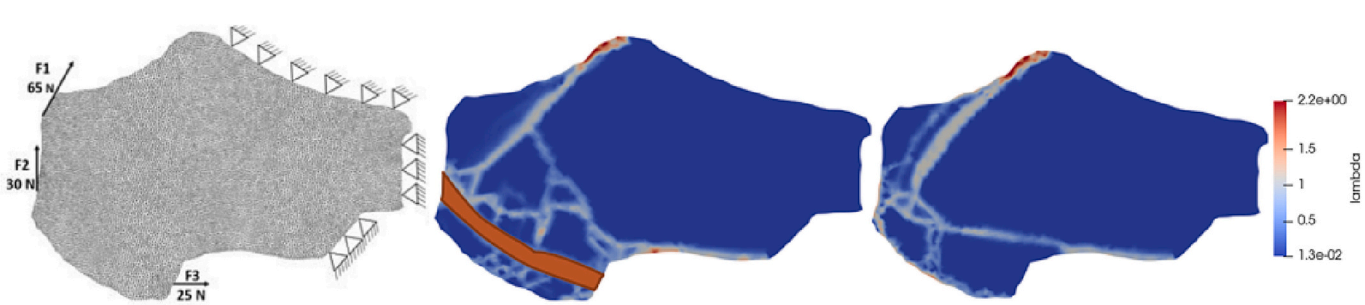

Fig. 6. Effect of growth plate presence on trabecular formations in the calcaneus.

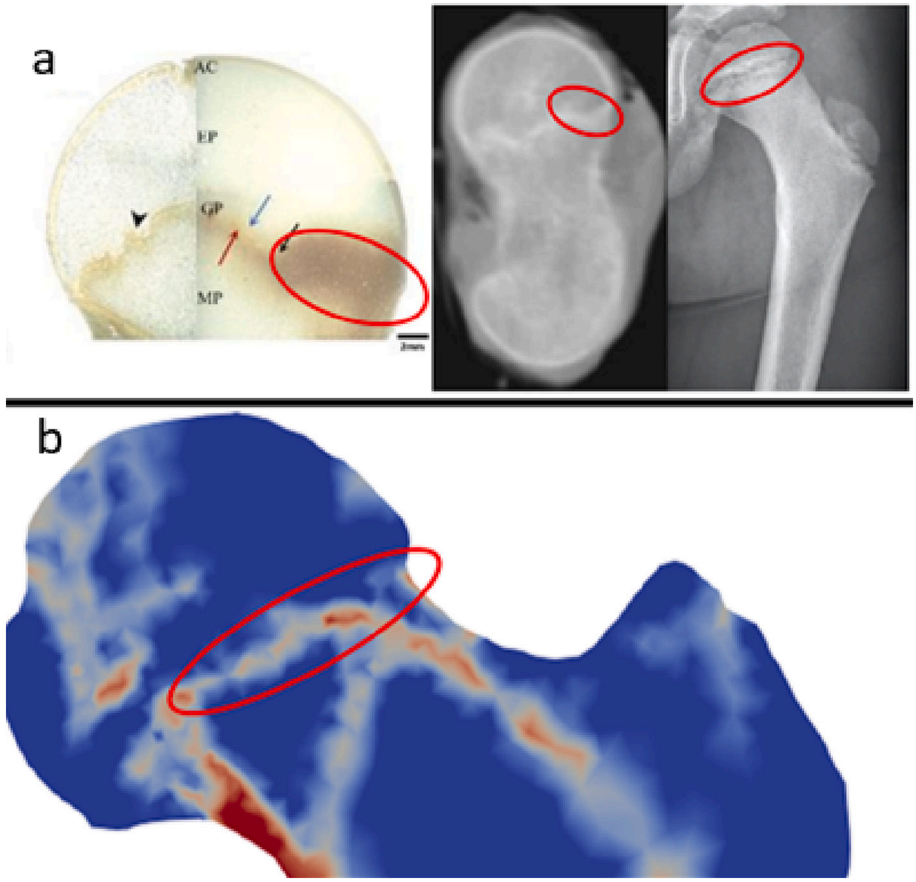

Fig. 7. a) Increased high density zones in proximal femur [20] b) Increased bony formation in high shear stress zones.

Data availability

Data will be made available on request.

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