Finite Element Modelling of the Foot for Clinical Application: a Systematic Review

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Abstract:

Over the last two decades finite element modelling has been widely used to give new insight on foot and footwear biomechanics. However its actual contribution for the improvement of the therapeutic outcome of different pathological conditions of the foot, such as the diabetic foot, remains relatively limited. This is mainly because finite element modelling is only been used within the research domain. Clinically applicable finite element modelling can open the way for novel diagnostic techniques and novel methods for treatment planning/optimisation which would significantly enhance clinical practice.

In this context this review aims to provide an overview of modelling techniques in the field of foot and footwear biomechanics and to investigate their applicability in a clinical setting.

Even though no integrated modelling system exists that could be directly used in the clinic and considerable progress is still required, current literature includes a comprehensive toolbox for future work towards clinically applicable finite element modelling. The key challenges include collecting the information that is needed for geometry design, the assignment of material properties and loading on a patient-specific basis and in a cost-effective and non-invasive way. The ultimate challenge for the implementation of any computational system into clinical practice is to ensure that it can produce reliable results for any person that belongs in the population for which it was developed. Consequently this highlights the need for thorough and extensive validation of each individual step of the modelling process as well as for the overall validation of the final integrated system.

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1. Introduction:

The ability to assess in vivo stresses that are developed inside the human foot during clinically relevant scenarios would significantly enhance our understanding on foot biomechanics and foot related pathologies. In the case of the diabetic foot, in particular, the ability to calculate internal stresses could shed new light on the phenomena that lead to ulceration and enable the optimisation of offloading strategies on a patient specific basis.

Despite this, there is no experimental method for the non-invasive assessment of internal soft tissue stress. Moreover, the complex geometry and nonlinear mechanical behaviour of the foot render any analytical solution practically impossible without significant simplifications in terms of morphology and function [1].

Finite element (FE) is a powerful numerical method which can be utilised to solve problems with complicated geometry, material properties and loading. Therefore it is no surprise that current literature is rich in elaborate FE analyses on foot and footwear biomechanics. FE analyses have already given new insights in the phenomena associated with ulceration of the diabetic foot [2–9] and the offloading capabilities of diabetic footwear [4,6,10]. However, the actual contribution of FE analyses for the improvement of the therapeutic outcome of the diabetic foot is relatively limited [11]. This is mainly because FE modelling cannot be utilised outside the research domain to enhance and inform the everyday clinical management of the diabetic foot, or other foot related pathological conditions [11].

One of the main challenges for the implementation of FE modelling in everyday clinical practice is the development of reliable and affordable techniques for the subject specific

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modelling of the foot. Although the ability to use any modelling technique in the clinic is mainly determined by its ease of use, its non-invasive nature and low cost, the potential to actually enhance clinical practice is determined to a great extent by the accuracy and relevance of the information it can provide. Therefore, the main purpose of this review is to provide an overview of different modelling approaches and simulation techniques that have been used in the field of foot and footwear biomechanics and to investigate their applicability in a clinical setting and where possible also to comment on their accuracy.

2. Method:

Relevant databases (Pubmed and Scopus) were searched using the keywords: (finite element [Title/Abstract]) AND (foot [Title/Abstract] OR shoe [Title/Abstract] OR plantar [Title/Abstract]) on 4th September 2015. The search was limited to studies with full texts published in English but there was no limitation in terms of publication date.

This review considered original papers on FE analysis of both the entire foot and parts of foot. In addition, FE analyses of footwear and insoles were also included. Analyses that were not focused on the entire foot or parts of the foot but on musculoskeletal structures proximal to the talus or the ankle joint were excluded. This means that studies on ankle, knee or hip prostheses/orthoses as well as studies on fracture and fracture fixation of the tibia and femur were all excluded. The papers which modelled foot with amputation were also excluded. After removing the duplicates, the abstracts of 322 articles were screened and 165 articles that met the criteria for inclusion based on abstract were selected. Full text of all remaining articles were then assessed against the eligibility criteria leading to the

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selection of 96 articles which met the inclusion criteria (Fig. 1). Selected papers were analysed in terms of the methods used for: a) geometry design, b) the assignment of material properties, c) the definition of boundary conditions and loading and d) validation.

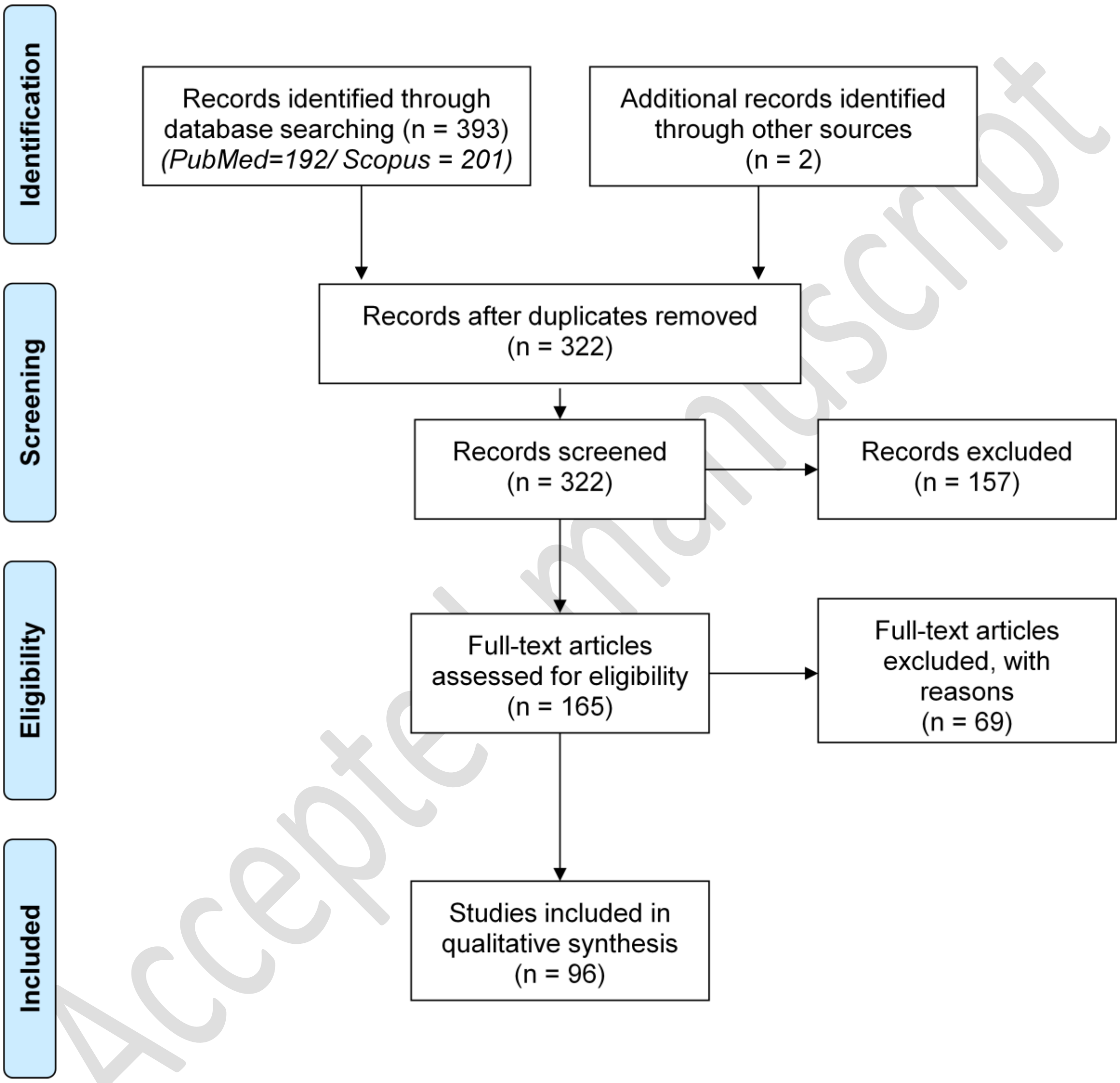

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Figure 1: Review flow chart (Prisma 2009).

These papers covered a wide range of applications in the broader area of foot biomechanics and used a variety of different simulation strategies. More specifically 79% of reviewed papers simulated the healthy foot and the remaining 21% the pathologic foot. Thirty three percent (33%) in total were focused on the interaction between foot and footwear and 13% were related to the diabetic foot. Detailed information about every study that was included in this review can be found in supplementary material (S1 Table).

3. Results:

The methods that were used in these studies for designing the geometry, assigning the material properties, defining loading and for validation are presented below. In each case specific methods and their applicability in the clinical setting will be discussed after a brief overview of the range of methods used.

3.1 FE model design

Two main methodological approaches were found for geometric design: The use of realistic representations of foot geometry (89% of reviewed papers) or the use of idealised geometry (11% of reviewed papers).

According to the first methodological approach the geometry is directly defined based on medical imaging through a segmentation and reconstruction process. Early approaches to the FE modelling of the foot utilised X-ray images [12–15] but almost all reviewed studies published after the year 2000 were based either on Magnetic Resonance Imaging (MRI), or Computer Tomography (CT) images (S1 table). Sixty four percent (64%) of these studies

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presented detailed 3D models of the entire foot [3,12–69] while 10% used detailed 3D models focused on specific parts of the foot [4,5,70–77]. Fourteen percent (14%) of reviewed studies developed 2D models of a cross-section of the foot based on a single CT/MRI image [2,6,10,78–88]. Finally only one study (1% of reviewed papers) presented a 2D model of a cross-section of the foot (frontal cross- section of the heel) reconstructed using ultrasound [89].

On the contrary idealised models of the foot entailed a simplified representation of geometry either assuming some type of symmetry or by simulating the tissues of the foot using basic geometrical shapes such as spheres, cylinders, etc. Eleven percent (11%) of the reviewed studies followed this approach [7,90–99] out of which only one study presented a 3D model [98].

3.1.1. Design of 3D realistic models of the entire foot

Geometry reconstruction:

Realistic models of the entire foot are usually reconstructed either from CT, which is more suited for imaging bones, or MRI which is more suited for soft tissues. CT and MRI were also combined in three studies to produce a more detailed reconstruction of both bone and soft tissues [30,51,69].

In the cases of CT and MRI, geometry reconstruction involves the segmentation of different tissues (e.g. bone, ligaments etc.) in a series/stack of images that corresponds to different sections/ slices of the foot. In most cases this process was performed manually or through semi-automated procedures and the use of specialised software (e.g. Mimics, ScanIP etc.).

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Based on that, it is clear that the reconstruction of the 3D geometry of the foot can be a very labour intensive task. In order to address this problem Camacho et al. [100] presented an automated method for the 3D reconstruction of the geometry of the bones of the foot from CT images. An automatic outlining tool was used to establish the border of each bone and this process was repeated for each slice containing the particular bone. The whole process was repeated for each bone using the talus as reference to determine their relative positions. The applicability of this method was demonstrated for a cadaveric foot and non-weight bearing conditions. Finally it should be noted that in their paper Camacho et al. [100] did not present information about the accuracy of their method.

A different solution to the same problem (i.e. the labour intensive nature of medical image analysis) was presented by Lochner et al. [24]. The authors of this study developed a generic anatomical foot model which was then modified to produce subject specific models. Skin surface geometry of the subject's foot was scanned and anatomical landmarks were identified and matched to those of the generic model reducing significantly the time needed to generate a patient specific model of the physiologic foot [24]. The applicability of this method was demonstrated using non-weight bearing imaging data from three subjects but similar to Camacho et al. [100], its accuracy was again not validated. Another limitation of this technique in the presented form is that it cannot be applied for “non-physiologic” feet (e.g. feet with a deformity such as hallux valgus etc.). Despite their limitations the aforementioned methods [24,100] highlight the need for automated algorithms to reduce the amount of work needed for geometry reconstruction.

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Besides the challenges related to the post processing of imaging data, the use of medical imaging itself can also impose serious limitations to the applicability of such methods in the clinical setting. More specifically one should also consider that both MRI and CT scanning are lengthy and expensive processes. In the UK, the cost of performing an MRI or CT scan can exceed £200 [101]. The costs normally relate to the scanning duration and the type of scanner. Whilst in many cases patients would be offered MRI or CT scans as part of their standard treatment plan, given the cost associated with these procedures it seems unrealistic to request them for the sole purpose of FE modelling.

One of the main determinants in terms of the duration of the scanning process, is the distance between imaged slices for the same total imaged area. Even though a variation of different imaging protocols were used in the reviewed papers, in all cases, the foot was imaged in the frontal plane and the distance between successive images/slices was less than 2 mm. Based on relevant experience within our team [102] such scanning process would take around 30 min to be completed. Finally, in terms of CT, one should also consider the risks associated with ionising radiation. .

Besides CT and MRI, X-ray imaging has also been used in a small number of studies [14,15,103,104]. Although X-ray imaging has some advantages over CT/ MRI in terms of cost and availability its use has been significantly limited mainly due to its significantly lower accuracy. X-ray imaging generates projected images of all tissues in its field of view which can make distinguishing different anatomical structures extremely difficult. As a result the geometry of 3D models produced using X-rays had to be significantly simplified, compromising their ability to produce reliable and clinically relevant results.

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Simulation of foot function:

One of the main challenges for the FE modelling of the foot is the simulation of the function of the foot's numerous joints. In order to address this challenge some authors bridged bones at the joints using a relatively soft material [3,31] enabling some relative movement between bones while others assumed contact between the opposite surfaces of the joints [30,105]. The use of contact elements could enable a more realistic simulation of joint function but at the same time it also significantly increases the computational cost and the complexity of the analysis.

In any case, different levels of complexity in the simulation of joint function were needed for studies with different objectives. The most elaborate and labour intensive approach for the simulation of joints was presented by Isvilanonda et al. [30]. The authors of this study combined CT with MRI images to get a more accurate reconstruction of both bone, which is more clearly seen in CT, and cartilage, which is more clearly seen in MRI. The joint interface conditions were simulated as contact with friction between deformable bodies (i.e. cartilage). This approach was deemed necessary because the joint function was considered to be very important for the purpose of this particular study, namely for the assessment of joint angle correction that can be achieved by different surgical techniques in the case of clawed hallux [30].

In total contrast to the aforementioned study Dai et al. [26] presented a 3D model of the foot where most bones were fused. The skeleton was encapsulated inside a bulk soft tissue which represented the outer morphology of the foot in detail. In order to recreate the

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overall bending stiffness of the foot, partition layers were cut at the major joints of the foot and linked with a material that simulated cartilage. In this case the aim of the FE investigation was to assess the effect of wearing socks on plantar soft tissue loading (i.e. plantar pressure and shear stress). For this purpose, the authors considered the overall bending stiffness of the foot to be more important than the function of separate joints [26].

Meshing:

Unfortunately, only a few studies presented details about the type of elements and density of mesh that was used. Based on the available information it appears that a 3D model of the entire foot requires at least ≈36,000 elements [59], while in some cases the total number of elements can be as high as 400,000 [55]. Based on these figures and considering the non-linear nature of most analyses (i.e. simulation of materials exhibiting non-linear mechanical behaviour, contact etc.) it becomes evident that one of the main disadvantages of geometrically detailed models is their high computational cost. Despite a clear trend for increasing available computational power the use of computationally "expensive" models would require specialised powerful computer units which would increase processing costs and lead to an increased time lag between testing and getting the results.

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3.1.2. Design of anatomically focused 3D models:

Geometry reconstruction:

In general, the focus of these analyses was on the plantar soft tissues of the forefoot [4,73,76] or rear foot [5,70–72,74,75,77]. These models were again reconstructed from MRI or CT images while the specific region that was modelled, was dictated by the aim of the study. Scanning a smaller area of the foot might reduce the duration of the scanning sequence but overall it is not expected to significantly reduce its cost.

Simulation of foot function:

Including only a part of foot anatomy into the model significantly limits the scenarios that can be simulated. Based on that, it is no surprise that all studies included in this category had objectives that enabled them to limit the analysis to very specific loading scenarios. For example: Budhabhatti et al. [4] aimed to comparatively assess the efficiency of different therapeutic interventions for plantar pressure reduction under the first ray of forefoot during “push off to toe off phase” [4]. An interesting method for the calculation of the initial configuration of the model was also presented here. More specifically, the authors of this study calculated the initial angle of the 1^{st} metatarsophalangeal Joint using an optimisation process to minimise the difference between in vivo measured and numerically calculated plantar pressure [4]. Similarly Fontanela et al. [75] designed a 3D model of the heel to simulate heel strike for barefoot and shod conditions and to analyse the interaction between the heel pad and different combinations of footwear materials.

Meshing:

In terms of meshing, only a handful of studies mentioned the number and type of element that were used. More specifically Budhabhatti et al. [4] performed a mesh convergence analysis and concluded that more than 10,000 8-node hexahedral elements were needed to minimise the effect of mesh density on the calculated peak plantar pressures for push off. On the other hand , Chokhandre et al. [72] used 30,576 hexahedral elements for their heel model while Fontanella et al. [5] used 400,000. Based on these it appears that focusing on

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specific areas of the foot doesn't necessarily lead to substantial reductions in the total number of elements. However, limiting the simulation to specific regions of interest can indeed reduce the overall computational cost of the analysis. For example focusing on the heel eliminates the need for simulating joint function which, as mentioned earlier, can be very computationally demanding.

3.1.3. Design of 3D idealised models:

To the knowledge of the authors of this review, the design and use of a geometrically idealised 3D model of the foot has so far been presented only in one study by Spirka et al. [98]. The aim of this study was to investigate the effect of different footwear designs on plantar pressure reduction.

Geometry reconstruction:

Spirka et al [98] developed a 3D model of the metatarsal head area of the foot using a combination of rigid spheres and cylinders to simulate the geometry of the metatarsal bones. The dimensions and relative position of these shapes was measured from CT images. More specifically, the radii of the spheres and lengths of the cylinders were equal to the maximum measured widths of the metatarsal heads and the overall length of the metatarsal bones respectively. The rigid bone models were linked with tension only springs simulating ligaments [98]. The properties of the ligaments were assigned based on literature [40] and their location based on anatomy software (Primal Pictures 3D Anatomy Software). The model of the skeletal structure was embedded into a block of compliant material simulating the plantar soft tissue. Although in this case the model was manually designed, the presented methodology appears to have the potential to become automated.

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Simulation of foot function:

The loading conditions of the metatarsal head area were simulated by directly loading each metatarsal head sphere [98]. The amount of the imposed force on each sphere was first estimated from plantar pressure measurements and then modified manually to minimise the difference between the numerical and in vivo peak pressure under each metatarsal head. Despite the simplified geometry and function of the foot model a comparison between numerical simulation and in vivo measurements revealed a good agreement in terms of pressure distribution. Even though this doesn't reduce the value of detailed models, it highlights the importance of implementing simplifications that minimises the labour intensity and computational cost of the model with minimum effect on the reliability of results.

At this point it needs to be highlighted that the effect on reliability needs to be assessed in the context of each specific application. For example, the modelling approach by Spirka et al. [98] presented here appears to be accurate enough for applications where estimations of plantar pressure are needed (e.g. informing the design of footwear interventions etc.). However this approach [98] is unlikely to be accurate enough for applications focused on internal tissue stresses.

Meshing:

Simplifications in terms of foot geometry and function can significantly reduce the amount of work that is needed for the design and meshing of the model. Despite the fact that the

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total number of elements used is not mentioned, it is easy to assume that significantly less FEs are needed compared to a detailed 3D model of the same region therefore the computational cost significantly decreases.

3.1.4. Design of 2D models:

Geometry reconstruction:

The studies included in this category focused on specific cross-sections of the foot and reconstructed the geometry of the tissues of the foot based on a single 2D image. In order to achieve that the authors of these studies assumed either plain strain [2,10,80,85] or plain strain/ stress with thickness elasticity [6,89] or axisymmetry [7,96,97,99].

Yarnitzky et al. [93] aimed to develop a simulation technique for the patient specific modelling of the heel pad and the real time calculation of its internal stresses and strains. To achieve this they designed a 2D FE model of the heel based on simple measurements (i.e. heel pad thickness, calcaneus curvature) on a sagittal X-ray of the foot. The 2D model of the heel pad was then combined with a 2D analytical model of the entire foot for the calculation of patient specific loading and the estimation of internal stresses. The accuracy of this technique was assessed using a synthetic foot model comprising rigid plastic skeleton embedded into silicon cast of the foot. These tests involved direct loading of the ankle joint and the measurement of internal stresses of the silicon heel pad for different levels of compression. According to the results presented by Yarnitzky et al. [93], the difference between the measured internal stresses and the numerically estimated ones ranged between 6.3% and 17%.

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Whilst not all studies provided information about the source of the 2D image used to reconstruct the geometry of the foot, it appears that most of them used images from MRI [10,81] or CT [2] scans. Other than MRI and CT ultrasound imaging was also used in one study [89]. More specifically, a frontal ultrasound image of the heel (B-mode imaging using a linear array probe) at the area of the apex of the calcaneus was used to design a 2D model (plane stress with thickness) of the heel comprising a rigid calcaneus and a deformable heel pad. The geometry of the calcaneus and the thickness of the heel pad were reconstructed using the ultrasound image. The thickness of the simulated slice was set equal to the thickness of the ultrasound probe [89]. In contrast to CT and MRI, ultrasound is relatively easy to use, safe (both for the patient and the operator) and its cost is low. On the other hand ultrasound imaging offers relatively limited field of view with lower accuracy compared to MRI or CT and the quality of the images can be strongly affected by scanning technique. Another limitation of ultrasound is that it cannot penetrate bony structures and, therefore, can image only their outer surfaces which makes it better suited for the study of soft tissues (e.g. muscles, ligaments, tendons etc.). Besides its limitations ultrasound imaging is a very good candidate for applications that are focused on soft tissues that are close to skin such as the plantar soft tissues.

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Simulation of foot function:

2D modelling imposes significant limitations to the load scenarios that can be simulated because no out-of-plane forces or displacements can be imposed. Moreover, the joints (if simulated) have to be simplified having only one rotational degree of freedom around an axis which is always perpendicular to the simulation plane. A method to reduce the effect of these limitations is to focus on specific areas/section of the foot and specific loading conditions for which out-of-plane loading and movement is minimal. For example, Erdemir et al. [6] used a 2D model of a slice of the metatarsal head area with the simulation plane aligned with the axis of the metatarsal bone. This model was used to simulate a specific gait event approximating the time of the second peak in vertical ground reaction force. For this instance of gait it can be assumed that there are no off-plane forces, translations or rotations.

Computational cost:

As one would expect the computational cost of 2D models of the foot is considerably lower compared to 3D models. An extreme example for the low computational cost of 2D models is the heel pad model of Yarnitzky et al. [93] where only 150 nodes were used.

3.2. Assignment of material properties

In the case of bones, cartilage, ligaments and tendons material properties were exclusively assigned based on literature. On the contrary, the material properties of the soft tissues of the sole of the foot (i.e. fat pad, skin etc.) were assigned using a combination of different techniques including methods based on in vivo measurement for the calculation of subject specific mechanical properties. The specific constitutive models used to simulate the mechanical behaviour of the tissues of the foot and the methods for calculating and assigning their material properties and mechanical coefficients are presented below.

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The first thing that becomes clear from these analyses is the very wide range of values of material properties/ coefficients that has been used to simulate the same tissue. Erdemir et al. [7] investigated the effect of using non subject specific mechanical properties of plantar soft tissue on peak plantar pressure and found that using material properties that are averaged for a specific population may change peak plantar pressure by up to 7% compared to using a subject specific mechanical properties. These results clearly highlight the effect of the chosen materials properties on the obtained numerical results and the importance of using patient specific ones when possible.

3.2.1 Material models

Bone and cartilage:

Bone tissue was modelled in almost all studies either as rigid or a homogenous linearly elastic material with Young's modulus ranging from 7,000 MPa to 15,000 MPa. On the other hand cartilage was only modelled in 55% of the reviewed studies and in almost all of them it was simulated as linearly elastic with Young's modulus ranging from 1 MPa to 12MPa. Cartilage was simulated as hyperelastic material only in 4% of studies [38,51,69,76] and as a viscoelastic material only in one study (1% of reviewed papers) [62].

Whilst these studies covered a wide range of applications, it becomes clear that in applications where bone and cartilage deformations are minimal (e.g. due to low magnitude of loading) or irrelevant (e.g. studies focused on internal soft tissue stresses/ strains) the shape of skeletal structures is far more important than the realistic simulation of their

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mechanical behaviour. In contrast to the applications outlined above, one study aiming to investigate the effect of impact loading on leg injury modelled both bone and cartilage as viscoelastic materials [62]. Simulating the time-dependent aspects of the mechanical behaviour of tissues can significantly increase the computational cost of the analysis. Considering the aim of the aforementioned study and the highly dynamic nature of simulated loads [62] it becomes clear that in this case the added computational cost is necessary in order to achieve satisfactory accuracy.

Ligaments and tendons:

Ligaments were modelled in 62% of the reviewed studies. In the majority of these studies, ligaments were assumed to be linearly elastic with Young's modulus ranging from 11.5 MPa to 1,500 MPa. The non-linear mechanical behaviour of ligaments was taken into account only in 6% of studies using a 5^{th} order polynomial model [54,84,87,88] or as a viscoelastic model [58,62] or fibre-reinforced viscohyperelastic model [51,69,76]. Most studies that modelled ligaments paid special attention to the simulation of plantar fascia by using different properties relative to the rest of the ligaments. Tendons were modelled only in 15% of studies and in all of these cases they were simulated as linearly elastic with Young's modulus ranging from 15 MPa to 1,200 MPa.

Realistic simulation of the mechanical behaviour of ligaments and tendons is of paramount importance in studies which focuses on (1) ligament or tendon biomechanics [51,106], (2) the effect of pathological conditions [88] or (3) the efficiency of relevant treatments [30,58].Typical example of a FE analysis where the accurate simulation of ligament/ tendon

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mechanical behaviour is very important is the study by Isvilanonda et al. [30] where two different surgical techniques for the treatment of clawed hallux deformity were compared. In this case, the ligaments and tendons were simulated as hyperelastic materials. However, no clear evidence could be found which could indicate the best material model for each specific application and there are cases where different material models have been used to simulate similar scenarios. Considering the added computational cost and complexity that results from the use of more elaborate material models it needs to be highlighted that in every case the decision should be made through rigorous validation, based on the specific aims of the study and the level of accuracy that is needed in order to achieve such aims.

Soft tissues:

Seventy seven percent (77%) of studies in total considered some type of bulk soft tissue to simulate the combined mechanical behaviour of skin, fat and muscle. More specifically, 65% modelled all three soft tissues together while 8% merged skin and fat in a single bulk tissue and simulated muscle separately. On the contrary 4% of studies merged fatty layer and muscle into a bulk tissue and simulated skin separately.

Even though some studies considered this bulk tissue to be linearly elastic (E=0.15MPa – 1.15MPa) [3,12–15,17,18,21–23,26–30,37,42,43,45,46,64–66,93,106–109] in most cases the mechanical behaviour of the combined muscle and fatty layer was simulated as hyperplastic using the Ogden material models. In all these cases bulk soft tissue was assumed to be incompressible or nearly incompressible (Poisson's ratios of 0.45-0.49). The use of these models required assigning values to a minimum number of two material coefficients in the

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case of incompressible 1st order Ogden material [7,72] to a maximum number of six in the case of 5th order polynomial material model [84,87].The viscous nature of the soft tissues of the sole of the foot was also simulated using a visco-elastic [58,95] or a visco-hyperelastic [70] constitutive model. In the aforementioned cases of visco-elastic and visco-hyperelastic models a minimum number of two [95] to a maximum of five [70] coefficients had to be defined.

Skin was simulated as a separate tissue in 20% of reviewed studies [2,5,31,36,51,56,59–61,69,71,73–77,83,85,94] . In these studies skin was mainly simulated as isotropic hyperplastic using the Ogden [71,73,77,83], Neo-Hookean [60,61] Jamus-Green-Simpson [94] or 2nd order polynomial [2,56] material models. A more elaborate model was used by Fontanella et al. and also Forestiero et al. who simulated skin as fibre-reinforced anisotropic hyperelastic material [5,69,75,76]. On the contrary a more simplified approach was followed by Shin et al. and Luboz et al. who simulated skin as having a linearly elastic mechanical behaviour [31,59]. The number of material coefficients that the authors had to define for the aforementioned models was one for incompressible Neo-Hookean, two for incompressible Ogden hyperelastic [71,73,77], five coefficients for the Jamus-Green-Simpson and six coefficients for the 2nd order polynomial [2] and the fibre reinforced hyperelastic material models [5,75,76].

Fat pad was simulated as a separate tissue in 19% of reviewed studies [2,5,31,36,51,59–61,69,71,73–77,83,85,94]. In most of these studies fat tissue was simulated using the Ogden hyperplastic model while its visco-hypelastic nature was only simulated in 5% of studies

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[5,51,69,75,76]. The visco-hyperelastic model that was used in these cases required assigning values to twelve material coefficients in total [5,51,69,75,76].

Muscle was simulated as a separate tissue only in 9% of studies [19,38,59–62,73,86] using either the Ogden [73] or the Mooney Rivlin [19,38] or neo-Hookean [60,61] models. In a more simple approach Luboz et al. [59] simulated muscle as linearly elastic.

A critical analysis indicates that studies focused on bone fracture, fixation and healing [19,27,86] or the biomechanics of ligaments and tendons [21,22,30,37,38,45,65,109] are unlikely to need nonlinear material models for the simulation of plantar soft tissue mechanical behaviour. In these cases the assumption of linear elasticity appears to offer satisfactory accuracy for the intended use of the models. In other cases and especially where the focus is on internal plantar soft tissue stresses/ strains the use of more elaborate material models appears to be very significant.

In the case where a more accurate simulation of plantar soft tissue biomechanics is needed, the most commonly used material model is the 1st order Ogden hyperelastic model. This model appears to enable accurate simulation of the nonlinear nature of the mechanical behaviour of plantar soft tissue and reliable estimation of plantar pressure with the minimum number of material coefficients [7,72,89,110,111]

3.2.2 Subject specific material properties

Despite the fact that for most tissues (e.g. ligaments, tendons, cartilage etc.) the calculation of subject specific mechanical properties is extremely difficult, the reviewed studies include

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in vivo measurement based methods that enable the calculation of subject specific properties for the soft tissues of the sole of the foot. These methods are implemented in two steps namely: in vivo testing and coefficients calculation.

In vivo testing:

The two most commonly used in vivo tests for the material characterisation of plantar soft tissue is indentation [7,68,77,82,89,94] and compression [5,73]. In the case of indentation, a rigid indenter with dimensions that are significantly smaller than the tested area is pressed against the plantar aspect of the foot. The applied force is measured using a load sensor which is in series with the indenter while tissue deformation is assessed either based on indenter displacement [12,77] or the real-time measurement of indenter-to-bone distance [7,68,82,89]. In the latter case the plantar soft tissue is loaded using an ultrasound probe which plays the role of the indenter (i.e. ultrasound indentation).

In the case of compression, the rigid surface that is used to load the foot has similar or larger area than the loaded area of the foot. Similar to indentation, in this case tissue deformation is either calculated based on the displacement of the compression plate [5] or directly measured using medical imaging [73]. The effect of the size of indenter on the reliability of indentation results was numerically investigated by Spears et al. [112] who concluded that indenters with bigger footprints can produce more reliable and robust measurements of the stiffness of the heel-pad.

Coefficients' calculation:

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The most common technique for the calculation of the nonlinear material coefficients of plantar soft tissue is inverse FE analysis [7,20,73,89,94,99]. According to this method a FE model of the in vivo test is used to calculate the values of the tissues' material coefficients that minimise the difference between in vivo and numerical results. To this end, Erdemir et al. [7] performed ultrasound indentation tests at the heel using a cylindrical indenter. These tests were then simulated using axisymmetric FE models comprising a bulk soft tissue with subject specific thickness. An optimisation algorithm was utilised to find the values of two nonlinear material coefficients (Ogden 1^{st} order) that minimise the difference between the numerical and in vivo force/deformation curves of the indentation test [7]. In order to improve the subject specificity of the inverse engineering process Chatzistergos et al. [89] loaded the foot using a linear array ultrasound probe and reconstructed the geometry of the calcaneus in the field of view from B-mode images. In this case the indentation test was simulated using a plane stress with thickness model comprising a bulk soft tissue with subject specific thickness and geometry [89]. An optimisation algorithm was used to inverse engineer the material coefficients of heel-pad.

A more elaborate approach was followed by Petre et al. [73] who used a custom made device to compress the forefoot inside an MRI scanner. The compression test was then simulated using subject specific 3D FE models of the forefoot comprising rigid bones and layers of different soft tissues (i.e. skin, fat and muscle). The geometry of these models was reconstructed from the MRI images of the unloaded foot while the MRI images of the loaded foot were used to assess internal deformations of different layers of soft tissues. At the end, an optimisation algorithm was used to minimise the difference between the numerically calculated and the in vivo measured internal deformations. This approach

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enabled the calculation of six material coefficients in total (i.e. two coefficients per tissue layer) [73]. The results of this study also indicated that realistic representation of the internal structure of plantar soft tissues is needed in order to achieve a more accurate estimation of internal tissue stresses/ strains [73]. This finding highlights the importance of simulating the inhomogeneity of plantar soft tissue in order to achieve satisfactory accuracy in applications that are focused on the accurate estimation of internal plantar soft tissue stresses/ strains.

It is clear from the aforementioned studies that there is a limit to the number of coefficients that can be inverse engineered from indentation or compression tests. Moreover, increasing the material coefficients that need to be calculated can also significantly increase the overall analysis time of the inverse engineering process [111] by increasing the number of iterations that are needed to reach final solution. To overcome these problems some authors combined in vivo testing with the use of in vitro data from literature [5,77]. For example, Fontanella et al. [5,113] used data from in vitro tests to get a first estimation of the twelve coefficients for their visco-hyper-elastic model of the heel pad and then used in vivo compression tests performed at different loading rates to adapt the values of six of these coefficients.

A significantly more simple approach was followed by Thomas et al. [12] in a study aiming to assess the effect of stiffening of plantar soft tissue on its internal stresses in people with diabetes. For this purpose a standardised durometer was used to measure Shore hardness at the heel. The elasticity modulus of heel pad was directly estimated from Shore hardness using a previously published relationship that links the shore hardness of cartilage to its

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modulus of elasticity [114]. Even though this technique is by far the most easy to use, it is non-invasive and computationally efficient it is highly unlikely that it can achieve the desired levels of accuracy especially in terms of estimation of internal tissue stresses/ strains.

Considering the challenges around the calculation of subject specific material properties, it is clear that the potential for clinically applicable modelling is significantly enhanced in applications where the required accuracy can be achieved with the use of generic or population specific properties instead of subject specific ones [115]. An application of FE modelling that appears to fulfil this criterion is the optimisation of the cushioning properties of bespoke insoles [89]. In this context, a numerical study performed by Chatzistergos et al. [89] indicated that the stiffness of an insole that minimises plantar pressure is not affected by the stiffness of plantar soft tissue. In contrast to patient specific tissue mechanical properties patient specific loading was found to have a very strong effect on the optimal cushioning properties of insoles [89].

3.3 Loading:

Loading within the reviewed studies, in the main, was applied in the form of external (i.e. ground reaction force) or internal forces (i.e. muscle forces) or a combination of both (S1 table). The values of these forces were calculated either based on body mass, or in vivo measurements or using musculoskeletal modelling.

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3.3.1 loading scaled based on body mass

Forty three percent (43%) of the reviewed studies calculated the forces that are imposed on the foot model as a percentage of body weight (BW) based on literature. Most of the studies simulated balanced standing by applying 50% of BW on the centre of pressure or the ankle joint. Studies that considered muscle forces applied 25% BW to the Achilles tendon [16,17,21,27,28,32,34,44–46]. The reported in literature percent of BW that is applied to the Achilles tendon was increased to 37.5% BW in two studies to improve agreement with in vivo measurements in terms of plantar pressure [23,65].

Another technique for the simulation of balanced standing is to separately calculate the loading that is imposed to different parts of the foot. This technique was used in the case of 2D models simulating different rays of the foot [2,84,87,88] but also in the case of 3D models [19,38] aiming at a more realistic distribution of foot internal loading. In these cases the calculation of individual loading for each foot array was based on data from Simkin [116] according to which the total load carried by the foot can be distributed as 25%, 19%, 19%, 19%, 18% from first to fifth ray respectively [116].

3.3.2 Loading based on in vivo measurements:

Twenty six percent (26%) of the reviewed studies directly measured ground reaction forces using force plates, pressure mats or in-shoe pressure sensors to define the magnitude of the imposed loading. Assigning loading directly from measured ground reaction forces appears to be very relevant for studies focusing on specific regions of the foot and specific phases of gait offering reliable estimations of plantar pressure. A typical example for this approach is

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the study by Budhabhatti et al. [4] where subject specific toe off ground reaction forces were measured using a force plate and then were applied to a subject specific 3D model [4].

Moreover, the use of accurate measurements of subject specific loading seems to be very relevant for studies focused on foot/ footwear interactions and plantar pressure reduction. As mentioned earlier this was highlighted in a numerical study by Chatzistergos et al. [89] where loading magnitude was found to be the most important factor for the optimisation of the cushioning properties of insole materials.

In order to calculate subject specific internal forces (i.e. ankle joint forces and the plantar fascia tension) Yarnitzky et al. [93] combined in-shoe measurements with an analytical model of the foot. The authors aimed to develop a simulation technique for the patient specific modelling of the heel pad and the real time calculation of its internal stresses and strains. For this purpose they designed a 2D FE model of the heel based on simple measurements on a sagittal X-ray of the foot (i.e. heel pad thickness, calcaneus curvature). The 2D model of the heel pad was then combined with a 2D analytical model of the entire foot which was used to estimate the force vectors in the Achilles tendon, plantar fascia, plantar ligament and tibio-talus joint [93].

All FE analyses are based on either assumed or measured loads to calculate internal tissue stresses and strains. This fundamental characteristic of FE analysis means that FE models cannot directly predict adaptations in gait and therefore in tissue loading as a result of altered internal tissue properties or stresses/strains. In order to overcome this limitation, Hollaran et al. [78,80] combined musculoskeletal modelling with optimal control and FE

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modelling. More specifically the authors of these studies used a 2D musculoskeletal model of trunk and lower limbs comprising seven rigid segments, eight muscle groups which were coupled with a 2D (plain strain) model of the 2nd ray of the foot. The two models were coupled at the ankle joint with the musculoskeletal model passing to the FE model the vertical position and orientation of the ankle joint and the FE analysis calculating and returning to the musculoskeletal model the ankle joint reaction forces. The prediction of changes in gait was performed using an optimal control algorithm which searched for gait patterns that satisfy the conditions of the problem (e.g. periodicity, constant walking speed etc.) and at the same time minimised a cost function. This cost function was defined in a way that enabled among others the minimisation of muscle "fatigue" and the minimisation of the intensity of plantar soft tissue loading. Despite limitations such as high computational cost (i.e. reported computation time of 10-14 days) this novel approach highlights the potential of combining different modelling regimes (i.e. musculoskeletal modelling with optimal control and FE modelling) to predict adaptations in gait due to mechanical changes in tissues, or to indicate how gait could be altered to change the way tissues are loaded to prevent injuries or promote rehabilitation. Despite this there is no information provided on the in vivo validation of this method.

3.4 FE model validation:

Validation is of paramount importance for any clinically relevant application of FE modelling but at the same time it remains one of the most challenging aspects of computational biomechanics. Indicative of this is the fact that 44% of the reviewed studies did not present any kind of validation (S1 table). The studies that did include validation (56%) compared

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numerical results against in vivo or in-vitro experimental data (i.e. direct validation) or against data from literature (i.e. indirect validation).

In the case of indirect validation (6% of the reviewed studies) the numerically estimated plantar pressures [50] or stress/strain behaviour of specific tissues [2,31,35,93] was compared to respective data from literature [2,31,35,38,50,93].

In the case of direct validation against in vivo data, the majority of studies used barefoot or in-shoe plantar pressure distribution and/or peak plantar pressure. Besides that, one study compared numerically calculated ground reaction forces against in vivo measured ones [88] and one more study compared numerical and experimental displacements of specific bones using direct motion capture and reflective markers [46].

4. Discussion

This review highlights that a number of fundamental challenges still exist and a considerable progress is still required before patient specific FE analysis can become a clinical tool for the management of diabetic foot or other foot pathologies. The key challenges in terms of model design, material properties assignment and loading are described below and possible available solutions are discussed. Considering the fact that achieving satisfactory levels of accuracy is the ultimate deciding factor for the clinical applicability of any numerical technique, methods for direct validation are disused separately at the end of this section.

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4.1 Model design

The first key challenge towards clinically applicable FE modelling is collecting reliable information for geometry design/ reconstruction in a cost effective and non-invasive way. Based on the reviewed studies, it is clear that the two most commonly used imaging modalities for this purpose is CT and MRI. This is because CT and MRI offer superior image quality enabling the accurate reconstruction of bone or soft tissue geometry respectively. Based on that it is clear that in the case of applications and pathological conditions where CT and/or MRI are already included into the patients' standard treatment their use to support FE modelling would clearly be the best option.

Besides that, in cases where CT and/or MRI are not part of the standard treatment plan of patients requesting them solely for modelling purposes seems impractical. In these cases ultrasound imaging with its low cost, low risk for patients and high availability in clinics appears to the best alternative imaging modality to support FE modelling [89]. Considering the limitations of ultrasound in terms of depth of field-of-view, contrast and bone imaging it becomes clear that its use will have to be restricted to applications focusing on soft tissues close to the surface of the foot, such as skin, fat pad etc. Moreover, concerns about user dependency will also have to be addressed. The development of automated ultrasound scanning systems for the foot can enhance reproducibility and minimise user dependency phenomena.

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X-ray and surface topography have also been used to reconstruct the geometry of the foot. In the case of X-ray risks with regards to the use of ionising radiation and the difficulties in distinguishing overlapping anatomical structures have significantly limited its usage. On the other hand surface topography offers a relatively quick, cost effective and accurate reconstruction of the 3D geometry of the external surfaces of the foot. However the fact that it cannot offer any information on the internal structure of the tissues of the foot makes its stand-alone use for the design of FE models of non-physiologic feet very challenging.

The second key challenge is being able to accurately reconstruct tissue geometry in a non-labour intensive way and without the need for specialist knowledge. Most of the reviewed studies employed specialised software for the manual segmentation and 3D reconstruction of tissue geometry. In contrast to this approach reliable automated techniques are required to reconstruct tissue geometry with minimum user input. For this purpose two automated techniques for the design of 3D models of the foot were identified. According to the first one, an automatic outlining tool was used to segment bones in a series/stack of CT images produce 3D objects by combining the bone outlines of successive slices [100]. The second solution employed a generic model of the foot which was modified and adapted to match the external geometry of the subject's foot [24]. Although these two studies highlight the potential for automated geometry reconstruction techniques, to the knowledge of the authors of this review, these methods have not been yet validated nor used in big cohort studies indicating that substantial further development is needed.

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The third key challenge related to model design is minimising the computational cost associated with FE analyses to enable immediate feedback on results without the use of specialised high performance computational units.

The computational cost of FE simulations increases with the size of the model and the complexity of the analysis. In general, the size of a FE model corresponds to the total number of equations that need to be solved in each step/ iteration (i.e. total number of degrees of freedom), which in turn depends on the type and total number of elements in the model. On the other hand complexity is linked to the number of steps/ iterations that are needed to get the final results of the analysis (i.e. the number of times that the aforementioned equations need to be solved). Starting from a simple linear analysis where solution is achieved in one step/ iteration the simulation of any nonlinear or time dependent phenomenon can significantly increase computational cost by significantly increasing the number of solution steps/ iterations that are needed in order to reach the final solution. Specifically in the case of the reviewed studies, the computational cost is significantly increased by the use of materials with nonlinear and/or time dependent mechanical behaviour (e.g. hyperelastic materials, viscoelastic etc.) and by the use of contact elements.

Despite the fact that not all studies provided information about the computational cost of their models it is clear that detailed 3D models of the entire foot will include a significant number of degrees of freedom. This, combined with the non-linear nature of the analyses

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and possible need for contact elements to simulate joint function will make performing the analyses very challenging without using specialised high performance systems. Two generic approaches were identified to reduce computational cost, namely the design of anatomically focused models or the design of simplified/ idealised ones. The studies following the first approach designed highly specialised models of parts of the foot (e.g. heel) simulating very specific loading scenarios (e.g. heel strike). By significantly limiting the range of scenarios that the model can simulate, the authors of these studies were able to design anatomically detailed models of parts of the foot and reduce the models' degrees of freedom [4,5,70–77] and in some cases eliminate the need for simulating joint function [5,70–72,74,75,77]. Based on the published data it is clear that drastic reduction in computational cost can only be achieved through radical simplifications in tissue geometry and foot function [26,89,93,98].

At this point it needs to be re-iterated that accuracy is the ultimate deciding factor for clinical applicability. Considering that accuracy and minimal computational costs are two objectives that are usually mutually exclusive means that the actual target for future developments in this field should be finding methods that can achieve satisfactory accuracy with the minimum possible computational cost and not simply minimising computational cost.

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4.2 Assignment of material properties

All biological tissues exhibit complex non-linear and time depended mechanical behaviour which makes their simulation inherently difficult. The majority of the reviewed studies assigned material properties based on literature. Whilst identifying the right material model and properties from the wide range of possible options in literature could be adequately difficult the real challenge is being able to estimate material properties on a patient specific basis. To achieve that, a combination of in vivo mechanical testing and advanced computational and/ or mathematical analysis techniques is required. Moreover it is clear that in order for these techniques to be applicable in the clinic, in vivo mechanical testing will have to be non-invasive and easy to perform in a clinical setting and the techniques for the calculation of material properties should be robust and fast.

In this context, the reviewed studies included methods that can only be used to calculate patient specific material properties of plantar soft tissues. These methods were based on two similar types of non-invasive mechanical tests, namely indentation and compression, using custom made loading devices designed specifically for this purpose. The combined use of these loading devices with MRI or ultrasound imaging, can significantly enhance the reliability of the measurements by enabling the direct measurement of internal tissue deformations [7,73,89]. Moreover the use of medical imaging opens the way for separate material characterisation of different tissues, namely skin, fat etc. instead of the common practice of characterising only a bulk plantar soft tissue [73]. To this end, the techniques like ultrasound elastography may be used to differentiate between the different layers of soft tissue in terms of the differences in density and deformability.

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In addition, these studies highlight the potential for patient specific characterisation of plantar soft tissue mechanical behaviour [7,73,89]. However the actual techniques used, appear to be better suited for lab-based applications rather than for use in clinics. Building on the existing techniques special attention needs to be paid to develop affordable in vivo testing systems that are safe and easy to use in the clinic. Specialised devices that require the patient to stand or rest their feet on a scanning surface to produce a map of the mechanical properties of plantar soft tissues would have significantly higher chances of being integrated into clinical practice compared to existing compression or indentation devices. Considering recent advances in the fields of weight bearing foot scanners, ultrasound imaging and elastography the development of such scanning device seems feasible.

In terms of the computational aspects of tissue mechanical characterisation, the reviewed studies highlighted the use of inverse engineering from in vivo testing mainly using optimisation driven procedures. These iterative methods are associated with high computational cost which can significantly limit their clinical applicability. A possible solution to this problem is the use of surrogate models that can be trained to predict the output of FE analyses thus considerably reducing the computational cost of the inverse engineering process [117]. At this point, it needs to be stressed out that the reliability of these surrogate models is still to be proven, especially in wide cohorts, therefore it is fair to say that a considerable amount of work is still needed to ensure validity and accuracy before deciding the applicability of such techniques in the clinic.

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4.3 Loading

One of the main challenges in terms of defining boundary conditions and loading for the models is being able to assign clinically relevant loading without the need for specialised equipment and time-consuming measurements. According to literature, the simplest methods to calculate loading appear to be a scaling based on literature or previous normative measurements using the patient's body weight. However, it is clear that calculating loading using this approach would limit the patient specificity of the analysis.

In cases where accurate measurements of truly patient specific loading are critical for the reliability of the analysis, measurements of ground reaction forces using force plates, pressure mats or in-shoe pressure sensors could be used to directly inform loading in the form of externally applied forces [75] or a combination of external and internal forces [93].

4.4 Validation

The ultimate challenge for the implementation of any FE modelling system into clinical practice is to ensure that it can produce reliable models for any person that belongs in the population for which it was developed. This means that the accuracy of every part of the modelling process as well as of the entire process as a whole will have to be assessed in wide cohort studies to validate their accuracy for populations rather than just for individuals. These validation tests will not have to be implemented in the clinic as part of day-to-day practice which opens the way for more elaborate, thorough and at the same time time-consuming and expensive approaches, such as the combined use of medical imaging and custom loading devices to study internal tissue deformations [9,118].

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Besides validating the ability of the entire process to generate reliable models for specific populations, additional validation protocols for each individual patient will also be needed. In this case simpler validation protocols will be needed that can be implemented in the clinic without significantly increasing the time and cost of the whole process. For this purpose more basic pressure based validation approaches could be used (see section 3.4).

5. Conclusion

The review clearly highlights the potential for the currently available models to be utilised in a clinically applicable fashion. This is specifically the case where the FE models were used to identify the mechanical properties of the plantar soft tissue for diagnostic purposes and in identifying the effect of footwear on an individualised basis. This has been facilitated by the practicality of using simplified geometry (that is not necessarily feasible in other areas of FE application i.e. corrective bone surgeries) which can significantly reduce computational cost as well as the amount of information that is needed for model design. Furthermore the ability to quantify subject specific geometry and material properties through techniques such as ultrasound elastography that can be easily implemented in a clinic promises new possibilities in the area of diagnostics and prescription.

Finally, this review highlights the need for thorough and extensive validation of each individual step of the modelling process as well as the validation of the final integrated system. As indicated in this review, the ultimate challenge for the implementation of any

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computational system into clinical practice will be to ensure its accuracy not just for a small group of people but for the entire population for which it was developed.

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<u>Supplementary material caption:</u>

S1 Table: The database of studies that met the inclusion criteria and were included in this review. Detailed information about the methods used for model design, material assignment, loading and validation is presented. The studies are presented in alphabetical order based to the surname of the first author.

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