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Best methods and data to reconstruct paediatric lower limb bones for musculoskeletal modelling

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Abstract:	<p>Background: In biomechanical simulations, generic linearly scaled musculoskeletal anatomies are commonly used to represent children, often neglecting or oversimplifying subject-specific features that may affect model estimates. Inappropriate bone sizing may influence joint angles due to erroneous joint centre identification. Alternatively, subject-specific image-based musculoskeletal models allow for more realistic representations of the skeletal system. To this end, statistical shape modelling (SSM) and morphing techniques may help reconstructing bones rapidly and accurately. Specifically, the Musculoskeletal Atlas Project (MAP) Client, which employs magnetic resonance imaging (MRI) and/or motion capture data to inform SSM and non-rigid morphing techniques, proved able to accurately reconstruct adult pelvis and femur bones. Nonetheless, to date, the above methods have never been applied to paediatric data.</p> <p>Methods: In this study, paediatric pelvis, femurs and tibiofibular bones were reconstructed using the MAP Client. Ten different combinations of SSM and morphing techniques, i.e., pipelines, were developed. Generic OpenSim bone geometries from the gait2392 model were linearly scaled for comparisons. Jaccard index, root mean square distance error and Hausdorff distance were computed to quantify reconstruction accuracy. For the pelvis bone, colour maps were produced to identify areas prone to inaccuracies and hip joint centres (HJC) location were compared. Finally, percent difference between MRI- and MAP-measured left-to-right HJC</p>	

distances were computed.

Findings: Pipelines informed by MRI data, alone or in combination with motion capture data, accurately reconstructed paediatric lower limb bones. Scaled OpenSim geometries provided the least accurate reconstructions. Principal component-based scaling methods produced size-dependent results, which were worse for smaller children.

1 Introduction

Musculoskeletal (MSK) models are powerful tools that can be used to investigate the internal biomechanics of the human body (Delp et al. 2007; Marra et al. 2015). Combined with experimental data (e.g., ground reaction forces and motion capture, MOCAP, data). MSK models can simulate locomotion (Delp et al. 2007) and estimate muscle forces and joint contact forces (JCF) (Moissenet et al. 2014). MSK models thus provide an alternative to invasive methods, such as instrumented implants (Fregly et al. 2012a), and have the potential to assist clinical decision making via virtual surgery planning (Delp et al. 1990; Fregly et al. 2012b) and predictive simulations (Jonkers et al. 2003). Nonetheless, there are a number of considerations that need to be taken into account when interpreting results from MSK modelling simulations.

Commonly used MSK models are based on generic skeletal anatomies gathered from small cohorts of healthy older adult (male) subjects (Delp et al. 1990). Routine personalisation involves linear scaling to resize generic bony geometries to each individual's dimensions. However, the further an individual's anthropometry differs from the generic model (e.g., small stature, deformity), the more likely their scaled model will be an inaccurate anatomical representation. Inaccurate bony geometries will consequently affect joint definitions by altering the location of joint centres (Bahl et al. 2019; Gerus et al. 2013; Lenaerts et al. 2008), which in turn will affect joint angle and joint moment calculations (Kainz et al. 2017a). Furthermore, muscle attachments may be inappropriately positioned (Duda et al. 1996), leading to erroneous muscle-tendon units (MTU) length and moment arm estimates (Scheys et al. 2011; Scheys et al. 2008) ultimately affecting predicted muscle function (Garijo et al. 2017; Heller et al. 2003; Passmore et al. 2018). Fortunately, subject-

specific image-based MSK models (Blemker et al. 2007; Bosmans et al. 2014; Murray et al. 1998; Passmore et al. 2018) may overcome these problems.

Subject-specific bone reconstructions can be obtained via segmentation of medical images (Blemker et al. 2007; Brito da Luz et al. 2017). Magnetic resonance imaging (MRI) and computed tomography (CT) are commonly employed for qualitative and quantitative assessment of bones in clinical settings (Eckstein et al. 2006; Hong et al. 2000; Oei et al. 2016). Alternatively, new technologies, such as EOS (Melhem et al. 2016) and 3D ultrasound (Parmar et al. 2010; Treece et al. 2003), may be used for imaging purposes to reduce time, costs and exposure to radiation. However, segmenting medical images is often a manual and time-consuming process, with the exception of CT scan segmentation that can be fully automated (Cootes et al. 1995; Krčah et al. 2011). Nonetheless, MRI images are more appealing for many MSK modelling applications compared to CT scans, which are characterised by inferior soft tissue contrast (Sharma and Aggarwal 2010) that prevents individual muscles segmentation. Moreover, cartilage, ligaments and other soft tissues may not be visible on CT scans (Hayashi et al. 2016). Upon segmentation, reconstructed three-dimensional bony geometries may be employed to generate subject-specific skeletal models (Valente et al. 2017), enabling the investigation of subject-specific joint kinematics and joint kinetics (Brito da Luz et al. 2017). However, muscle origin and insertion points are not embedded in such bone models. Therefore, if muscle forces and JCFs are to be studied, muscle attachments and muscle pathways would need to be manually defined.

Statistical shape modelling (SSM) and morphing techniques, such as host-mesh fitting (HMF) and local-mesh fitting (LMF) (Fernandez et al. 2004), are alternative methods to manual segmentation of bones from medical images. The open-source software Musculoskeletal Atlas Project (MAP) Client (Zhang et al. 2014b) combines SSM and fitting methods to reconstruct lower limb bones and allows for the customisation of the gait

OpenSim MSK model (Delp et al. 1990) with personalised bony geometries. Furthermore, since each MAP generated bone embeds information on muscles attachments, the resulting customised MSK model can be directly employed to estimate muscle forces and JCFs. Within the MAP Client, mean statistical shape bone models, resulting from a database of 26 adult lower limbs (and over 200 femurs), are typically morphed along a set of principal components (PCs) in order to minimise the error between correspondent landmarks/measurements on the mean model and on experimental data (i.e., medical images or MOCAP data). However, all PCs currently implemented in the MAP Client were extracted from the above adult dataset. As such, the MAP Client may not be able to accurately reconstruct paediatric bones whose shapes and sizes are not comprised in the training adult population. To improve bone reconstructions (i.e., increase accuracy of bone models), segmentations of medical images (be those MRI or CT scans) may be used to inform and guide the morphing process via HMF and LMF techniques. The underlying idea is that the more data provided, the better the reconstructions. Nevertheless, incomplete segmentations potentially provide sufficient information to accurately reconstruct adult femur and pelvis geometries (Nolte et al. 2016; Suwarganda et al. 2019; Zhang and Besier 2016). To date, the accuracy of paediatric bone models produced from the MAP Client has not been investigated

We systematically set out four aims to determine the most accurate methods to reconstruct paediatric pelvis (without sacrum), femurs and tibiofibular bones using SSM and morphing techniques. (1) Determine whether linear or non-linear approaches are best for scaling lower limb paediatric bones, (2) determine whether incomplete sets of MRI data could be used to improve scaled bone geometries, (3) investigate the benefits of including mesh fitting methods to correct for possible inaccuracies derived from scaling approaches and (4) investigate the effect of reconstruction inaccuracies on hip joint centre estimates. To this end, we implemented ten different combinations of morphing techniques, henceforth referred

to as pipelines, in the MAP Client that were informed by MOCAP data only, MRI data only or by a combination of both MOCAP and MRI data. Furthermore, both complete and sparse segmentations were evaluated to identify the minimum MRI data required for accurate scaling. We hypothesised that (H1) pipelines employing PC-based methods would not produce satisfactory results when applied to a paediatric population, (H2) incomplete sets of medical images would be sufficient to enable accurate bone reconstructions, (H3) providing both MOCAP and MRI segmentations would improve results and (H4) that pelvis reconstruction accuracy, as determined by hypotheses H1-3, would be related to improved hip joint centre estimates.

2 Material and Methods

2.1 Participants

Data from 18 typically developing children were included in the study (Height: 144.78 ± 16.24 cm, age: 10.78 ± 2.78 years, Table 1). All procedures were approved by the institutional Research Ethics Committee and informed consent was provided.

2.2 Data collection and processing

Fifty-one retro-reflective MRI-compatible surface markers were placed on anatomical landmarks (Table 2) by an experienced motion capture physiotherapist. Marker trajectories were collected using a 10-camera motion capture system (Vicon Motion System, Oxford, UK, 100 Hz) with subjects standing in T-pose (Cappozzo et al. 1995). Motion capture data were cleaned and labelled in Vicon Nexus 2.5, then processed in MATLAB using the MOtoNMS toolbox (Mantoan et al. 2015). Trajectories were filtered using a 4th order 6 Hz low-pass Butterworth zero-lag filter. Finally, hip, knee and ankle joint centres were computed for scaling purposes. Hip joint centres (HJCs) were determined using the Harrington equation (Harrington et al. 2007), while knee and ankle joint centres were defined as the midpoint

between medial and lateral knee condyles and medial and lateral malleoli markers, respectively.

Medical imaging data were acquired as part of separate research projects on two different MRI scanners. Fifteen participants' images were acquired on a Magnetom Siemens 1.5 T (thickness: 1.0mm, voxel size: $0.83 \times 0.83 \times 1.0 \text{ mm}^3$), while for the remaining 3 children, a Philips Insigna 3T was used (slice thickness: 1.0 mm, voxel size: $0.79 \times 0.79 \times 1.0 \text{ mm}^3$). In both cases, full lower limb MRI scans were acquired with the subjects laying supine, employing sequences specifically optimised for identification of bone contours.

Bony structures were manually segmented from MRI data using the Mimics Research Suite v20 (Materialise, Leuven, Belgium). For each participant, the pelvis (excluding sacrum), left femur, and left tibiofibular bones were segmented using the multiple slice edit tool to define bone borders from which the volume was determined. To balance quality of segmentations and time consumption, bone contours were segmented finely (i.e., every other slice) in correspondence of complex shapes (e.g., femur head or the whole pelvis structure) and coarsely along the bone shafts where changes in shape were minimal and automatic contour interpolation could work well. All segmentations were then exported in stereolithography (STL) format.

2.3 Bone reconstruction using the MAP Client

The open-source plug-in-based software MAP Client (Zhang et al. 2014b) was used to reconstruct paediatric lower limb bones by combining several SSM and morphing techniques. These included linear and non-linear PC scaling, HMF and LMF.

Linear scaling was informed by either MOCAP or MRI data. When using MOCAP data, linear scaling was performed as per OpenSim guidelines (Delp et al. 2007; Hicks et al. 2015). Selected bony landmarks (i.e., left and right anterior superior iliac spine; hip, knee and

ankle joint centres) were used to calculate the scaling factors for each bone dimension by computing the ratio of Euclidean distances between virtual anatomical landmarks on the MAP model and corresponding MOCAP markers. Landmarks pairs for scaling were defined as per Kainz and colleagues' (2017b) recommendations. When using MRI data, linear scaling was performed using an iterative closest point algorithm, in which the SSMs were rigidly scaled to minimise the root mean square distance error (RMSE) between closest points on the MAP bone and on the corresponding MRI segmentation meshes. Although a better match in size was ensured, the original shape and curvature of the mean MAP SSMs were not altered.

Medical imaging and MOCAP data were also used to drive non-linear PC scaling. In this case, a user-defined number of PCs were employed to determine the directions along which to deform each mean MAP SSM. The goal was to minimise the distance error between (i) MOCAP markers and corresponding virtual landmarks on the morphed MAP model or (ii) nodal points on MRI and MAP bone point clouds, for MOCAP- and MRI-informed pipelines respectively. Principal components were used to explore the whole range of shape variations within the MAP atlas, enabling a better fit of SSMs to experimental data. In accordance with previous studies (Nolte et al. 2016; Suwarganda et al. 2019), non-linear scaling employed four PCs to morph pelvis and femur bones and eight PCs for the tibiofibular bone when informed by MRI data. On the other hand, non-linear scaling methods informed by MOCAP data, which morphed all lower limb bones at once, used five PCs. Five PCs were identified as ideal to minimise distance error while using a least number of components since only small reductions in distance errors were observed when reconstructing adult pelvis and femur bones after increasing the number of PCs from four to five. User defined weighting factors (i.e., Mahalanobis distance) were set to guide the morphing process aiming to achieve a low final RMSE (i.e., below 2 mm), which ensured that the resulting morphed SSM properly fit experimental data, providing an acceptable approximation of the real bone.

Mesh fitting techniques were finally used to refine bone reconstructions. Both HMF and LMF fitting methods aimed to reduce nodal points distance errors between MAP bone models and corresponding MRI segmentations. HMF primarily improved on the overall shape of the bone by morphing nodal points while preserving the relative distance between them. LMF worked on a point-by-point base allowing for localised refinements. In a coarse-to-fine refinement fashion, HMF was performed prior to LMF. Method-specific weights and penalties (i.e., 2D and 3D Sobolev and boundary normal smoothing terms) were employed to preserve natural shapes and smoothness (Suwarganda et al. 2019).

2.4 Pipeline development

The identification of the best combination of methods to generate paediatric lower limb bones with the minimal amount of data and highest level of accuracy followed a step-wise process composed of four main tests. The first test involved comparing linear and non-linear PC scaling approaches using MOCAP or MRI to assess which method resulted in best bone reconstruction. The second test assessed how different levels of MRI data sparsity (Fig. 1) affected bone reconstruction.

Fig. 1 Different levels of medical imaging data provided to the MAP Client. Full (a) and incomplete (b-c) MRI segmentations used in the MRI-informed pipelines

The third test assessed whether shape and curvature reconstruction inaccuracies could be corrected via pipelines involving combinations of morphing techniques (Fig. 2). The fourth and final test assessed the error between HJC estimated by each pipeline and real HJC as determined from MRI data.

Fig. 2 Pipelines developed and tested to reconstruct paediatric lower limb bones. Each pipeline, identified by the number above it, comprised different steps, represented in circles. Different colours refer to different methods/techniques employed. Shades of green or blue

indicate MOCAP-based and MRI-based methods, respectively. Pipeline 0 was performed in OpenSim on generic geometries from the gait2392 model. Pipelines 1-10 were run in the MAP Client. LS = Linear scaling, PC = Non-linear principal component scaling, HMF = Host-mesh fitting, LMF = Local-mesh fitting

2.5 Pipelines summary

Ten different pipelines (Fig. 2) were developed to explore the scenarios where only MOCAP data, only medical imaging data, or both, were available. Moreover, to identify the minimal amount of imaging data required to accurately reconstruct paediatric bones, both sparse and complete segmentations (Fig. 1) were used to inform the MAP Client. For additional comparisons, in pipeline 0 all bones were reconstructed using OpenSim's MOCAP linear scaling approach on generic bone templates from the gait2392 model (Delp et al. 1990). For consistency, the same landmarks pairs were selected in OpenSim and the MAP Client to compute each bone's linear scaling factors. All pipelines were run on a desktop computer (i.e., Intel Core i5 @ 3.50GHz, 4 Cores), and in general, the more steps included in a pipeline, the longer the computational time required to reconstruct all bones of interest (Table 3).

3 Data Analysis

Bones reconstructed using the MAP Client were compared to the corresponding full MRI segmentations using different metrics (Fig. 3).

Fig. 3 Metrics used to assess the accuracy of reconstructed bones. Volumetric (a) and surface (b) similarity indices between each reconstructed MAP bone and the corresponding MRI segmentation were computed using the reported formulas (bottom right). For the pelvis, colour maps (c) were produced to understand how the surface error was distributed

First, the Jaccard index (JI) defined as the ratio between the intersection and the union of two volumes was used to determine volume similarity (Fig. 3a). Second, the RMSE was computed to quantify surface reconstructions inaccuracies. Third, the Hausdorff distance, defined as the maximal surface-to-surface distance error between point clouds (Fig. 3b), was used to identify inaccurate reconstructions. Furthermore, for the pelvis bone, which was characterised by a more complex structure in comparison to femurs and tibia/fibulas, visual checks were performed to understand how the distance error was distributed on the bone surface (i.e., evenly or in specific locations). To this end, colour maps of the MAP-to-MRI distance error were produced (Fig. 3c). Finally, HJC (left and right) locations were determined and compared to the centres of the spheres fitted to the acetabula on MRI segmentations. The inter-HJCs distance and percent error between MRI and MAP Client measurements were also calculated and compared to results from Harrington's regression equation, commonly used in clinical practice. Finally, to determine possible effects of participants' size on bone reconstruction accuracy when using non-linear PC scaling methods, a linear regression model (numpy.polyfit module in Python 2.7) was fitted to individual JI values for all reconstructed lower limb bones. The slope of each regression line (i.e., β), R^2 and p values were computed to extract further information on the quality of the fit.

4 Statistical analysis

All data were tested for normality. If the data distributions were normal, comparisons between pipelines were performed via repeated measures ANOVA tests. Otherwise, the equivalent non-parametric tests (i.e., Friedman test followed by Wilcoxon signed rank tests) were used. To account for multiple comparisons, the significance level, initially set to $p < 0.05$, was recalculated implementing Bonferroni corrections. All analyses were performed in the Statistical Package for the Social Sciences version 25 (SPSS Inc., Chicago, USA).

5 Results

All results are reported in Tables 4, 5 and 6. The first test involved the comparison of linear and non-linear PC scaling methods. For all tested bones, pipeline 3, solely employing linear scaling approaches and MRI data, produced more accurate geometries than pipeline 5, which combined linear and non-linear scaling methods, and pipelines 0-2, which were informed by MOCAP data alone (Fig. 4).

Fig. 4 Volume similarity between bones reconstructed in the MAP Client using scaling approaches and corresponding MRI segmentations for the pelvic, left femoral and left tibiofibular bones. Bar graphs report Jaccard indices as mean values across the studied population (n=18) for the pipelines solely employing linear or non-linear scaling methods, i.e. P0-6. Different shades of colours were used to separate pipelines performing one only scaling step (blue), or multiple scalings (red and purple). PC = Non-linear principal component scaling, LS = Linear scaling. Symbols denote significant differences: *compared to OpenSim LS, **compared to MOCAP LS, ^compared to MRI LS

Pipeline 4 performed similarly to pipeline 3, while pipeline 6, despite being associated with the highest mean JI (Fig. 4 and Table 4) for pelvis and femurs, generated abnormally shaped pelvis and tibiofibular geometries for small children (Figs. 5 and 6).

Fig. 5 Examples of pelvis bone reconstructions for one subject using the developed pipelines. Reconstructed pelvis and relative surface error distribution are reported via colour maps, where darker reds denote larger errors, expressed in mm. For completeness, Jaccard indices are reported in the grey circles. The labels PC and LS describe the type of scaling employed, i.e. non-linear principal components or linear scaling

Fig. 6 Jaccard indices as function of subjects' height. Individual Jaccard indices and corresponding fitted regression lines to show the relationship between reconstruction

accuracy and subjects' height for pipelines employing principal component-based scaling. Different colours refer to different pipelines. Black dashed lines represent results from pipeline 1 (lower line) and pipeline 9 (upper line), for comparisons. PC = Non-linear principal component scaling, LS = Linear scaling, HMF = Host-mesh fitting, LMF = Local-mesh fitting

This size-dependency was also noticed in results from pipelines 2 and 5, both employing non-linear PC scaling methods: the smaller the child, the worse the reconstruction. Regression lines fitted to individual JIs showed $R^2 = 0.60$ and 0.80 for pelvis, $R^2 = 0.55$ and 0.73 for tibia/fibula, using pipelines 2 and 5, respectively, versus $R^2 \sim 0$ from pipeline 1. Fig. 6 and Table 5. For children smaller than 145 cm, non-linear scaling methods produced less accurate reconstructions than linear scaling approaches and vice versa for taller participants (Figs. 5 and 6). Visual checks of the pelvis reconstructions revealed that, for small children, more natural shapes were produced when MAP Client geometries were scaled linearly rather than non-linearly (Fig. 5). Also, iliac crests and ischia (i.e., posterior inferior iliac spines, close to the acetabulum) were the areas of the pelvis more prone to reconstruction inaccuracies (Fig. 5). Moreover, linearly scaled femurs and tibia/fibulas from OpenSim were the furthest distance away from the actual bone segmentations ($JI_{Femur} = 0.54 \pm 0.05$, $JI_{TibiaFibula} = 0.55 \pm 0.06$ versus $JI_{Femur} > 0.65 \pm 0.05$ and $JI_{TibiaFibula} > 0.61 \pm 0.12$. Table 4). On the other hand, the pelvis bone was equally poorly reconstructed by all MOCAP based pipelines, as evidenced by the overall lowest volume ($JI_{Pelvis} = 0.20 \pm 0.08$, 0.26 ± 0.08 and 0.26 ± 0.13 ; from pipeline 0, 1 and 2, respectively) and largest surface ($RMSE \geq 8$ mm and Hausdorff distance ≥ 25.8 mm. Table 4) similarity indices.

The second test assessed the effect of MRI data sparsity on bone reconstruction. On the two best pipelines from test one (i.e., pipeline 3 and 4), different levels of incompleteness

were tested (Fig. 1 and Table 4a). The use of complete MRI segmentations was generally associated with higher similarity indices compared to both incomplete medical imaging datasets (Table 4). However, for the pelvis, there were no statistically significant differences between reconstructions from sparse and full segmentations ($p > 0.5$), while joint scans produced poorer results ($p < 0.018$). Conversely, for femurs and tibia/fibulas, joint scans enabled to reconstruct bones with higher levels of accuracy compared to sparse scans ($J\text{I}_{\text{Femur}}^{\text{joint}} = 0.69 \pm 0.05$ versus $J\text{I}_{\text{Femur}}^{\text{sparse}} = 0.67 \pm 0.05$ and $J\text{I}_{\text{TibiaFibula}}^{\text{joint}} = 0.70 \pm 0.06$ versus $J\text{I}_{\text{TibiaFibula}}^{\text{sparse}} = 0.68 \pm 0.07$).

The third test assessed whether freeform deformation techniques could correct shape and curvature inaccuracies observed in bone reconstructed via pipelines 4-6 (Table 4b). Pipeline 7, solely informed by MRI-data and employing linear scaling, HMF and LMF techniques, produced highly accurate bone geometries (Table 4). Pipelines 9 and 10, which were informed by MOCAP data and MRI segmentations, also produced very accurate reconstructions for all tested bones ($J\text{I}_{\text{Pelvis}} = 0.89 \pm 0.03$ and 0.84 ± 0.08 , $J\text{I}_{\text{Femur}} = 0.96 \pm 0.01$ and 0.94 ± 0.04 , $J\text{I}_{\text{TibiaFibula}} = 0.88 \pm 0.09$ and 0.94 ± 0.01). However, Wilcoxon signed-rank tests showed that employing a linear scaling step, in pipeline 9, as opposed to a PC scaling step, in pipeline 10, significantly improved reconstructions ($Z = +3.288$, $p = 0.001$). RMSE values were progressively smaller when more information was provided (Table 4). The smallest RMSEs (i.e., 1.53 ± 0.39 mm, 1.79 ± 0.47 mm and 1.55 ± 0.36 mm for pelvis, femur and tibia/fibula respectively) were obtained combining MOCAP and MRI linear scaling, HMF and LMF techniques (i.e. pipeline 9). On each reconstructed pelvis (Fig. 5), the largest distance error, decreased in value when more data were provided to the MAP Client (i.e., pipelines 9-10 versus pipelines 1-2 and complete versus incomplete segmentations, Table 4). The most accurate geometries were produced employing full segmentations, however joint

scans and sparse segmentations provided enough information to accurately reconstruct long bones and pelvis, respectively (i.e., JI around or above 0.8).

The fourth test assessed the ability of each pipeline to accurately estimate HJC location. Hip joint centres mislocation varied quite considerably across pipelines (Fig. 7).

Fig. 7 Dependency of hip joint centres location on subject's heights. Hip joint centres estimated from the different pipelines are displayed as spheres of different colours (red to fuchsia) overlayed to the correspondent MRI segmentation. Grey spheres indicate the reference hip joint centres derived from MRI segmentations. Orange circles on the scale at the bottom denote the subjects whose pelvis is displayed

When no segmentations were provided the error was the largest (17.66 ± 6.76 mm, 16.65 ± 7.27 mm and 15.10 ± 5.26 mm for left HJCs; similar values were found for the right HJCs). On the other hand, pipelines 7 and 9 were associated with the smallest location errors, i.e. 3.09 ± 1.47 mm and 3.01 ± 1.57 mm respectively (Table 6). For taller children, HJCs estimates from the different pipelines were clustered around the reference locations identified on MRI segmentations. Nonetheless, the smaller the participant, the larger the differences between pipelines (Fig. 7). The absolute percent inter-HJC distance error between MRI and reconstructed pelvis was largest for MOCAP linearly scaled geometries, both in OpenSim and the MAP Client (i.e., $22.31 \pm 10.38\%$ and $22.33 \pm 11.43\%$, respectively), decreasing (i.e., $\leq 9.26 \pm 6.03\%$) when medical images were provided and minimal (i.e., $1.92 \pm 1.70\%$) in pipeline 6 which was solely informed via MRIs (Table 6). Finally, pipelines 7 and 9 also produced significantly better estimates of left-to-right HJC distance compared to Harrington's regression equation (Harrington et al. 2007), which is commonly used in clinical gait analysis.

6 Discussion

In this paper, for the first time, the MAP Client was used to reconstruct paediatric lower limb bones. Ten different pipelines were developed and tested to determine the most effective combination of morphing methods and the amount of experimental data to be provided to ensure accurate bone reconstructions. Pipelines 7 and 9, which employed linear scaling methods and mesh fitting techniques, produced bony geometries with overall highest volume and surface similarity indices. Moreover, in agreement with our first two hypotheses, non-linear scaling methods were not able to accurately morph lower limb bones for small children (H1) and sparse and joint scans both enabled acceptable level of accuracy for pelvis and long bones (H2). On the other hand, contrarily to what we initially hypothesised (H3), the use of MOCAP data did not improve reconstruction accuracy, as pipelines 7 and 9 performed similarly. Finally, increased pelvis reconstruction accuracy was associated with more accurate estimates of HJC locations (H4).

As hypothesised, pipelines using non-linear PC approaches to scale bone geometries, e.g. pipeline 6, did not produce accurate reconstructions of paediatric lower limb bones. Abnormal pelvic and tibiofibular shapes were generated for children shorter than 145 cm (Fig. 5). Particularly, iliac crests and ischia, which correspond to the inferior and posterior regions of the pelvis, were the least accurately reconstructed regions (Fig. 5) of the pelvic bone. This finding is of practical importance for MSK modelling as several muscle attachments are located on the surface of these regions. Such size-dependent behaviour (Fig. 6) likely resulted from using PCs derived from an adult database (i.e., comprising subjects 160 to 180 cm tall), which presumably did not adequately describe variations within the shorter paediatric population. Nonetheless, for children taller than 145 cm, non-linear PC scaling produced more accurate reconstructions than linear scaling (Fig. 6 and Table 5). Therefore, for children of height above 145 cm, we recommend the use of pipeline 2 to

reconstruct paediatric lower limb bones if medical imaging data are not available, while for children shorter than 145 cm, pipeline 1 is preferred. More natural shapes, particularly for the pelvis and tibia/fibula, were produced for shorter children when linear scaling approaches were employed (Figs. 5 and 6, Table 4). Conversely, when MRI data are available, pipelines 3 should be preferred as it proved to better reconstruct paediatric lower limb bones compared to all MOCAP-based pipelines (Fig. 4 and Table 4). Linearly scaled OpenSim generic geometries were the least accurate overall ($Jl = 0.20 \pm 0.08$, 0.54 ± 0.05 and 0.55 ± 0.06 for pelvis, femur and tibia/fibula, respectively), suggesting that caution needs to be taken when interpreting the results from a generic OpenSim model that is scaled to the dimensions of a paediatric participant.

The use of full MRI segmentations to inform bone morphing, as expected, was associated with the most accurate reconstructions. Nonetheless, incomplete imaging datasets, which require less time and costs to be acquired, may provide sufficient information (Table 4) to accurately scale and morph bones without employing HMF and LMF techniques. However, different considerations need to be taken for each bone. For instance, the pelvis can vary considerably between individuals, even in healthy populations. Therefore, information from different areas (e.g., iliac crests, acetabula, ischia) may need to be provided to ensure accurate reconstructions, as reported by Suwarganda and colleagues (2019) and as shown in the present results. The use of joint scans, which did not carry information on the iliac crests, resulted in significantly poorer pelvis geometries compared to both sparse and full segmentations, which produced comparable results (Table 4). On the other hand, for femurs and tibia/fibulas, joint scans produced more accurate geometries than sparse segmentations. The possible reason being that joint scans included the whole bone epiphyses (Fig. 1), which may yield the largest degree of complexity compared to bone shafts for both femurs and

tibia/fibulas. However, more information may be required for pathologic populations presenting with deformity that impacts the mid-shaft (e.g., femoral torsion).

Combining MOCAP- and MRI-informed linear scaling, HMF and LMF methods, i.e. pipeline 9, led to the most accurate reconstructions of paediatric pelvis, femurs and tibiofibular bones both in terms of volume ($JI_{Pelvis} = 0.89 \pm 0.03$, $JI_{Femur} = 0.96 \pm 0.01$, $JI_{TibiaFibula} = 0.94 \pm 0.01$) and surface ($RMSE_{Pelvis} = 1.53 \pm 0.40$ mm, $RMSE_{Femur} = 1.79 \pm 0.47$ mm, $RMSE_{TibiaFibula} = 1.55 \pm 0.36$ mm) similarity to the MRI segmentations. More importantly, results were not size-dependent: low R^2 values (equal to 0.12, 0.39 and 0.56, Table 5) and minimal slopes were associated with the regression lines fitted to the Jaccard indices for pelvis, femur and tibia/fibulas reconstructions (Fig. 6 and Table 5). However, similar results were achieved with pipeline 7, which did not include the first MOCAP-based linear scaling step (Table 4 and Table 6), demonstrating that MRI data alone may be sufficient to generate accurate reconstructions. Moreover, pipeline 8, which employed non-linear PC scaling and has previously been associated with the highest JI for adult bones (Suwarganda et al. 2019), did not lead to similarly good results on paediatric data (e.g., $JI_{Pelvis}^{Paed} = 0.83 \pm 0.04$ versus $JI_{Pelvis}^{Adult} = 0.93 \pm 0.02$), most likely due to the use of PCs derived from an adult dataset. Once again, the use of full segmentations to inform the morphing process resulted in very high levels of accuracy, reported above, for all bones. However, in pipelines 7 and 9, good results ($JI > 0.8$) were also achieved when providing incomplete sets of medical images (Table 4). For long bones, which are characterised by simpler geometry compared to the pelvis bone, joint scans seemed to carry enough information to enable accurate reconstructions. Contrarily, for the pelvis, imaging data from the upper portion was still required for best results.

The benefits of employing imaging data to inform the morphing process and the limits of MOCAP-based pipelines to produce accurate reconstructions were further highlighted in

the fourth test which focussed on the pelvis bone. Pipelines 0-2 performed similarly to one another, i.e. poorly, and were associated with larger HJCs location errors ($\geq 15.10 \pm 5.26$ mm. Table 6) and abnormal inter-HJCs distances (i.e., up to 22% difference to the distance measured on MRI segmentations) compared to the other tested pipelines. However, in agreement with previously reported data (Bahl et al. 2019), HJC estimates were more accurate when imaging data were provided to inform the scaling and morphing processes (Table 6). Moreover, pipeline 0 and pipeline 9 produced results on opposite sides of the spectrum, with linearly scaled OpenSim geometries being the least accurate reconstructions overall and pipeline 9 the most accurate. Our results (Table 6) also showed that left-to-right HJC distances measured on the bones reconstructed using pipelines 6-9 were significantly closer to the MRI measurements compared to the both estimates from linearly scaled OpenSim bone models and via Harrington's regression equation (Harrington et al. 2007), which is the current gold standard in paediatric clinical motion analysis. Therefore, caution should be used in clinical gait analysis when computing HJCs location and distances using generic OpenSim scaling methods or via regression equations (e.g., Harrington formula), especially for smaller children (see Fig. 7). Such findings cannot be neglected when generating bones for use in MSK modelling applications, since errors in HJCs location may propagate to hip and knee joint angles calculations (Kainz et al. 2017a), possibly affecting subsequent joint kinetics computations and leading to misinterpretation of clinical findings.

It must be appreciated that accurately reconstructing pelvic, femoral and lower leg bones requires a large time investment (Table 3). For example, pipeline 9, which produced the most accurate reconstructions, took up to 7 hours per subject to run, including both computational time and the time to collect experimental MOCAP data, plus two to four hours for bone segmentations. On the other hand, pipelines 0-2, solely employing MOCAP data, required less than fifteen minutes to complete. However, pipeline 0 in OpenSim, which is

commonly used in research on paediatric populations and clinical practice, produced the worst reconstructions for all tested bones. Notably, the use of sparse segmentations allowed for reduced running time (~6 hours overall) without compromising reconstruction accuracy (e.g., $J_{\text{Pelvis}} > 0.80$). Importantly, the computational time here reported (up to 7 hours) may decrease in the future by using high-performance computers as opposed to standard office desktop machines. Finally, the ability to produce an accurate MAP Client bone model using medical image data only (pipeline 7) will facilitate investigation of human biomechanics ‘outside the lab’ through the use of inertial sensors (Pizzolato et al. 2017).

This study has limitations. Firstly, Jaccard indices are highly influenced by misalignment between MRI segmentations and correspondent MAP Client reconstructions. Despite a rigid registration process was used to minimise the RMSE between the point clouds, misalignment may have not been completely removed, negatively affecting results. Secondly, reported RMSE and Hausdorff distance values were calculated between pairs of closest points identified on the MAP Client and MRI segmentation meshes and computed in two ways, i.e. MAP-to-MRI and MRI-to-MAP, to account for errors due to inappropriate point picking. However, although the MAP Client meshes were discretised in order to have the same number of nodes as the corresponding MRI segmentations, the points may have not been similarly distributed, leading to larger distance errors in specific areas. It must be noted that both MRI and MAP Client meshes were finer at the bone extremities and coarser on the shafts for femurs and tibia-fibulas, while uniformly dense for the pelvis. Also, in some instances, MOCAP-based linear scaling failed to correctly resize the mean MAP Client model of the pelvis. This problem mainly affected pelvis width and may have been caused by the way multiple scaling factors are applied to a geometry within the MAP Client or erroneous experimental markers placements. To reduce the impact of MOCAP-based scaling errors, anthropometric measurements, e.g., pelvis width/depth, could be further provided to

the MAP Client to better inform the scaling process. Furthermore, to be consistent between participants, PC-scaling, HMF and LMF steps were iterated the same number of times across subjects and bones. However, this number may have not been ideal for all subjects, leading to suboptimal results. Finally, PC-based pipelines in this study used adult PCs, which were likely not ideal for paediatric bones. Future work should focus on populating a paediatric database to extract PCs capable of explaining the shape variations within a paediatric population.

7 Conclusions

Accurate reconstructions of paediatric pelvis, femur and tibiofibular bones can be generated combining SSM and morphing techniques. However, different approaches should be taken based on participants' height and availability of experimental data. For children of stature below 145 cm, non-linear scaling methods should be avoided until a population-specific database to extract paediatric PCs from is available. Pipelines which employ linear scaling approaches and that incorporate medical imaging data, should be selected to achieve optimal results. Contrarily, for taller children, PC-based pipelines may produce accurate results. In general, informing the morphing process with segmentations of medical images (via HMF and LMF) ensures accurate bone reconstructions. Full segmentations would ensure optimal results, however joint scans may be sufficient to reconstruct both femurs and tibia/fibulas, while for the pelvis bone to be accurately modelled more information (e.g. on the iliac crests) should be provided. Finally, MOCAP data alone to inform bone reconstruction may be insufficient and may lead to large HJCs location errors, ultimately affecting joint angles and joint moments estimates in MSK modelling simulations.

8 Conflict of interest

The authors declare that they have no conflict of interest.

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Figure 1

Figure 4

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Figure 5

Figure 7

Table 1. Demographics of participants. Age and height are reported as mean (standard deviation) across the studied population

Subject [ID]	Height [cm]	Age [years]
TD01	116	6.5
TD02	117	6
TD03	123.5	8
TD04	132.5	8.5
TD05	133	8
TD06	134	9
TD07	138.5	10.5
TD08	141	10
TD09	144	11
TD10	148	12
TD11	150	11
TD12	153	12
TD13	154	12
TD14	157	12
TD15	161	12
TD16	163	15
TD17	168.5	18
TD18	172	15
Mean(SD)	144.78(16.24)	10.78(2.78)

Table 2. Landmarks positions of the MOCAP markers. Anatomical landmarks name and location of the 51 retro-reflective markers affixed on each participants' body

Body segment	Marker name	Anatomical landmark
Back	C7	7 th Cervical Vertebra
	T10	10 th Thoracic Vertebra
	CLAV	Clavicle
	STRN	Sternum
	RBAK	Right back
Pelvis	L/RASI	Anterior superior iliac spine
	L/RIC	Lateral iliac crest
	L/RPSI	Posterior superior iliac spine
Knee	L/RKNE	Lateral femoral condyle
	L/RPAT	Patella
	L/RMKNE	Medial femoral condyle
	L/RLTC	Lateral tibial trochanter
	L/RTTB	Tibial tuberosity
	L/RMTC	Medial tibial trochanter
Foot	L/RANK	Lateral malleolus
	L/RHEE	Calcaneus
	L/RMMAL	Medial malleolus
	L/LMT1	Big toe
	L/RTOE	2 nd toe
	L/RMT5	5 th toe
Thigh	L/RTHI	Thigh wand marker
	L/RTH1-3	Thigh triad cluster
Shank	L/RTIB	Tibia wand marker
	L/RTB1-3	Tibial triad cluster

27 **Table 3.** Pipelines summary. List of morphing techniques employed and time required to complete each pipeline per subject

28

Pipeline	MOCAP		MRI			Time (Pelvis, Femurs and Tibia/Fibulas)
	Linear scaling	Non-linear PC scaling	Linear scaling	Non-linear PC scaling	Mesh fitting techniques	
0	✓					10-15 min
1	✓					10-15 min
2		✓				15-20 min
3			✓			~4 h
4	✓		✓			~4 h
5		✓	✓			~4 h
6			✓	✓		~5 h
7			✓		✓	10-12 h
8			✓	✓	✓	12-14 h
9	✓		✓		✓	10-12 h
10		✓	✓		✓	10-12 h

29

30 **Table 4a.** Volume and surface similarity metrics for pipelines solely employing linear or non-linear scaling methods. Jaccard index (JI), root mean
31 square distance error (RMSE) and Hausdorff distance values are reported as mean (standard deviation) across the population. In bold is highlighted
32 the pipeline which provided worst (red) results. For the pipelines employing MRI data, the letter in superscript indicates the level of segmentation
33 incompleteness: ‘j’ stands for joint scans segmentations while ‘s’ indicate sparse segmentations

Pipeline	Pelvis			Femur			Tibia/Fibula		
	JI	RMSE [mm]	HD [mm]	JI	RMSE [mm]	HD [mm]	JI	RMSE [mm]	HD [mm]
0	0.20(0.08)	12.57(1.63)	36.39 (9.32)	0.54(0.05)	7.43(1.13)	17.58 (3.00)	0.55(0.06)	8.16(1.22)	20.33 (2.87)
1	0.26(0.08)	8.45(3.10)	31.37(10.77)	0.65(0.05)	4.75(1.20)	14.98(4.46)	0.63(0.08)	4.27(1.20)	13.30(3.47)
2	0.26(0.13)	8.00(2.63)	25.79(8.28)	0.67(0.07)	4.29(0.78)	14.56(3.34)	0.64(0.09)	3.79(1.10)	15.24(9.96)
3_s	0.50(0.05)	4.00(0.81)	14.73(2.23)	0.66(0.06)	4.00(1.01)	12.58(3.63)	0.69(0.07)	2.86(0.55)	8.95(2.55)
3	0.51(0.06)	3.88(0.75)	14.56(2.33)	0.72(0.05)	3.62(0.57)	11.36(1.44)	0.72(0.06)	2.75(0.45)	8.58(2.01)
4_j	0.47(0.07)	4.38(1.20)	17.13(4.71)	0.69(0.05)	3.61(0.59)	11.72(1.66)	0.70(0.06)	2.79(0.49)	8.72(2.26)
4_s	0.50(0.05)	4.12(0.91)	15.69(3.35)	0.67(0.05)	3.81(0.64)	12.02(1.66)	0.68(0.07)	3.03(0.94)	9.57(3.60)
4	0.51(0.05)	3.89(0.70)	14.16(0.05)	0.71(0.05)	3.77(0.57)	11.50(1.33)	0.71(0.06)	2.76(0.44)	8.89(2.05)
5_j	0.31(0.11)	7.12(2.85)	26.69(9.85)	0.69(0.08)	3.67(0.87)	12.90(3.09)	0.63(0.11)	3.64(1.03)	14.37(8.28)
5_s	0.37(0.13)	5.66(1.70)	19.07(6.69)	0.67(0.09)	3.82(0.95)	13.18(2.68)	0.61(0.12)	3.86(1.55)	13.98(7.99)
5	0.38(0.12)	5.39(1.53)	17.61(4.66)	0.70(0.07)	3.81(0.78)	13.31(2.80)	0.65(0.09)	3.58(1.10)	14.47(10.34)
6_s	0.59(0.05)	3.45(0.38)	16.53(2.69)	0.68(0.19)	4.17(2.98)	16.16(11.83)	0.65(0.19)	4.90(5.17)	17.75(14.81)
6	0.63(0.05)	3.05(0.44)	14.64(2.58)	0.79(0.08)	2.92(0.79)	12.36(3.66)	0.70(0.19)	4.62(5.13)	15.66(14.42)

35 **Table 4b.** Volume and surface similarity metrics for pipelines employing linear or non-linear scaling methods in combination with mesh fitting
36 techniques. Jaccard index (JI), root mean square distance error (RMSE) and Hausdorff distance values are reported as mean (standard deviation)
37 across the population. In bold are highlighted the pipelines which provided best (blue) results. For the pipelines employing MRI data, the letter in
38 superscript indicates the level of segmentation incompleteness: ‘j’ stands for joint scans segmentations while ‘s’ indicate sparse segmentations

39

Pipeline	Pelvis			Femur			Tibia/Fibula		
	JI	RMSE [mm]	HD [mm]	JI	RMSE [mm]	HD [mm]	JI	RMSE [mm]	HD [mm]
7	0.89(0.03)	1.58(0.51)	10.05(3.40)	0.96(0.01)	1.78(0.47)	8.56(2.34)	0.94(0.01)	1.56(0.35)	6.82(2.52)
8 _s	0.74(0.05)	2.69(0.34)	15.60(3.64)	0.72(0.19)	3.87(3.00)	15.34(11.78)	0.68(0.18)	4.79(5.17)	17.65(15.11)
8	0.83(0.04)	1.95(0.37)	12.37(3.72)	0.92(0.03)	2.22(1.10)	11.18(6.83)	0.83(0.19)	4.15(5.27)	15.17(14.83)
9 _j	0.64(0.09)	3.69(1.21)	18.57(4.87)	0.87(0.04)	2.16(0.49)	9.37(2.11)	0.84(0.04)	1.88(0.29)	7.59(2.34)
9 _s	0.76(0.04)	2.83(0.69)	16.39(4.80)	0.78(0.03)	2.80(0.44)	10.56(1.37)	0.79(0.05)	2.18(0.48)	8.29(2.98)
9	0.89(0.03)	1.53(0.40)	9.75(2.84)	0.96(0.01)	1.79(0.47)	8.57(2.29)	0.94(0.01)	1.55(0.36)	6.77(2.51)
10 _s	0.56(0.16)	5.91(2.69)	31.12(12.71)	0.80(0.05)	2.82(0.57)	12.36(4.47)	0.76(0.09)	2.75(1.12)	12.60(7.42)
10	0.84(0.08)	1.98(0.60)	13.84(6.03)	0.94(0.04)	1.98(0.56)	10.14(3.31)	0.88(0.09)	2.27(1.28)	12.06(8.12)

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43 **Table 5.** Statistics of linear regression models. R-squared values (R^2), β coefficient (i.e. slope) and p-values (p) for the regression lines fit to the
44 individual Jaccard indices of pelvic, femoral and tibiofibular bones reconstructed using non-linear scaling methods. Higher slope values indicate
45 more pronounced size-effect on volume similarity. The colour code reflects the legend in Fig. 6

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Pipeline		Pelvis			Femur			Tibia/Fibula		
		R ²	β (slope)	<i>p</i>	R ²	β (slope)	<i>p</i>	R ²	β (slope)	<i>p</i>
1		0.007	-0.0004	0.736	0.008	-0.0003	0.731	0.005	0.0003	0.784
Non-linear PC scaling methods	2	0.600	0.0059	0.000	0.351	0.0024	0.010	0.450	0.0037	0.002
	5	0.787	0.0066	0.000	0.158	0.0016	0.103	0.552	0.0041	0.000
	6	0.350	0.0019	0.010	0.206	0.0021	0.058	0.689	0.0096	0.000
	8	0.672	0.0022	0.000	0.651	0.0016	0.000	0.630	0.0091	0.000
	10	0.660	0.0040	0.000	0.504	0.0017	0.001	0.733	0.0047	0.000
9		0.124	0.0006	0.152	0.391	0.0006	0.006	0.557	0.0006	0.000

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Table 6. Hip joint centers location and percent distance errors. Euclidean distances between left/right hip joint centres (HJC) and percent absolute inter-HJC distance error between MRI segmentations and registered pelvis reconstructions. Location errors are expressed in mm, while inter-HJC distance errors are reported as percent values. Hip joint centres distance was also calculated using Harrington equation, commonly used in clinical practice, and measured on MRI segmentations. Results are reported as mean (standard deviation). Significant differences ($p<0.05$) with respect to MRI measurements and from Harrington equation are indicated by the symbols ^ and * respectively. Superscript letters denote the level of MRI data sparsity: ‘j’ stands for joint scans segmentations, while ‘s’ indicate sparse segmentations

Pipeline	Left HJC error [mm]	Right HJC error [mm]	Inter-HJC distance Error (%)
Harrington	-	-	14.00(9.20)
0	15.10(5.26)	15.20(7.46)	21.26(11.78)
1	17.66(6.76)	17.60(7.25)	22.31(10.38)^
2	16.65(7.27)	16.69(7.90)	22.33(11.43)
3s	4.44(1.57)	5.00(2.73)	3.15(2.7)*
3	5.69(1.87)	5.83(2.99)	5.14(3.28)
4j	5.73(3.04)	6.54(2.79)	4.21(3.88)*
4s	8.60(6.90)	7.12(3.51)	6.28(6.25)
4	7.36(2.98)	8.39(4.17)	9.26(6.03)
5j	4.68(2.58)	5.27(3.01)	3.53(2.85)*
5s	5.06(2.11)	5.62(2.93)	3.79(2.86)*
5	6.04(2.06)	5.58(2.74)	5.14(3.41)
6s	3.40(1.36)	4.25(2.11)	1.98(1.87)*
6	3.50(1.44)	3.75(2.22)	1.92(1.71)*
7	3.01(1.57)	3.08(1.87)	2.96(1.68)*
8s	2.86(1.20)	2.70(1.75)	2.36(1.56)*
8	3.12(1.22)	2.77(1.75)	2.39(1.56)*
9j	3.22(2.42)	2.99(1.90)	2.93(1.81)*
9s	3.16(1.98)	2.98(2.43)	3.05(2.14)*
9	3.10(1.47)	3.08(1.80)	3.06(1.59)*
10s	7.48(4.32)	7.44(5.42)	7.99(7.61)
10	4.25(2.54)	3.58(1.75)	2.59(1.95)*

^ significantly larger than Harrington regression equation

*significantly lower than Harrington regression equation

Best methods and data to reconstruct paediatric lower limb bones for musculoskeletal modelling

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Abstract

Background: In biomechanical simulations, generic linearly scaled musculoskeletal anatomies are commonly used to represent children, often neglecting or oversimplifying subject-specific features that may affect model estimates. Inappropriate bone sizing may influence joint angles due to erroneous joint centre identification. Alternatively, subject-specific image-based musculoskeletal models allow for more realistic representations of the skeletal system. To this end, statistical shape modelling (SSM) and morphing techniques may help reconstructing bones rapidly and accurately. Specifically, the Musculoskeletal Atlas Project (MAP) Client, which employs magnetic resonance imaging (MRI) and/or motion capture data to inform SSM and non-rigid morphing techniques, proved able to accurately reconstruct adult pelvis and femur bones. Nonetheless, to date, the above methods have never been applied to paediatric data.

Methods: In this study, paediatric pelvis, femurs and tibiofibular bones were reconstructed using the MAP Client. Ten different combinations of SSM and morphing techniques, i.e., pipelines, were developed. Generic OpenSim bone geometries from the gait2392 model were linearly scaled for comparisons. Jaccard index, root mean square distance error and Hausdorff distance were computed to quantify reconstruction accuracy. For the pelvis bone, colour maps were produced to identify areas prone to inaccuracies and hip joint centres (HJC) location were compared. Finally, percent difference between MRI- and MAP-measured left-to-right HJC distances were computed.

Findings: Pipelines informed by MRI data, alone or in combination with motion capture data, accurately reconstructed paediatric lower limb bones. Scaled OpenSim geometries provided the least accurate reconstructions. Principal component-based scaling methods produced size-dependent results, which were worse for smaller children.

Keywords:

MAP Client; Bone reconstruction; Paediatric; Statistical shape modelling; Bone morphing