**Abstract** Costal cartilage bridges the sternum and the ribs and plays a key role in the biomechanics of the chest. Costal cartilage is known to calcify in local regions with age, which can substantially stiffen its overall response to loading. However, the rate of accumulation of the calcified volume is not well quantified. Current computational models of the thorax assign a homogeneous soft material to cartilage segments, yet their finite element meshes are well suited to the specification of interstitial calcification zones, should applicable data become available.

This study measures volumes and extents of costal cartilage calcification from 205 live subject CT scans. Significant increases in volume calcification – both in a given cartilage segment and in the lengthwise extent of those segments that experience calcification – are seen with age (p<0.0001). Age and sex accounted for 35% of all inter-individual population variability. Specific recommendations for introducing person-age via regional calcification to models of the costal cartilage are that (1) calcification volume within a segment should increase at the rate of 0.9 mm (for an equivalent cube edge length) per decade, and (2) should involve an increasing lengthwise extent of the cartilage segment at a rate of at least 7% per decade.

**Keywords** age, calcification, cartilage, costal cartilage calcification, rib.

I. INTRODUCTION

The chest plays a major role in mitigating the forces that the body experiences during motor vehicle crash events. Costal cartilage is a key structural component of the chest, contributing to its rigidity and reinforcing the chest wall by bridging the space between the sternum and the ribs. Simulated stiffening of the costal cartilage through an added tough outer shell has been shown to increase the overall chest stiffness by 50% [1], and simulated stiffening of the cartilage material itself has increased subsequent stress levels in the ribs by 63% during loading of the sternum [2] and increased rib fractures in diagonal belt loading [3].

Costal cartilage is organised in a series of segments connected to the ribs, with typical topology connecting ribs 1-4 directly to the sternum, ribs 5-7 to both the sternum and to superior segments, and ribs 8-10 to only superiorly neighbouring segments. Its material structure includes a hyaline cartilage mid-substance surrounded by an outer layer of perichondrium. Over time, portions of the costal cartilage can calcify (less commonly but more precisely termed ossify), producing inhomogeneities of substantially harder and stiffer material properties within or around a cartilage segment. This calcification can substantially stiffen the mechanical response of the cartilage, particularly when the calcified tissue forms a bridge across the length of a costal segment [4].

An association between advancing age and presence (or size) of calcification is well documented [5-9], and studies have also described differences between the typical patterns of calcification seen between males and females [8,10]. Results from these studies have been used forensically to help estimate the age and sex of unknown deceased persons [8,11]. However, with the most common data source being X-ray images taken from an anterior aspect, there is limited volumetric information describing the typical amounts and distribution of calcification that might inform 3D biomechanical models.

Computational human body models are increasingly being used to understand the biomechanics of the thorax to loading, and recent efforts have included the concept of person-age by building models specifically representing elderly individuals [3,12-14]. Forman and Kent [15] have highlighted the need for costal cartilage calcification to be considered when modelling changes in the mechanics of the rib cage with age, and have explored a methodology for the placement of calcified elements within current model meshes. One aspect still
lacking, however, is an understanding of how much of a given cartilage segment should be specified as calcified within a model in order to best represent the costal cartilage of a given demographic.

This study aims to contribute to the body of knowledge required to address that need by quantifying the volume and extent of cartilage calcification that is seen in adults, and to describe the population variability that exists for such measures. Specifically, this study aims to quantify the rate of calcification accumulation with age that is typical within a live adult population, and to quantify the differences in calcification amount that is expected between males and females. Such information can help build more accurate models of calcified cartilage in order to better understand the effect that age has on the biomechanics of the chest.

II. METHODS

Scan and Study Population
The study population consisted of 205 individuals (110 female, 95 male) aged 17 to 91 years. All subjects had received chest CT scans obtained for trauma purposes between 2001 and 2016, collected from the International Center for Automotive Medicine (ICAM) morphomics database. All scans were taken in a supine position. Scan axial resolution ranged from 0.56 mm to 0.97 mm, and scan slice spacing ranged from 0.625 mm (53% of scans) to 5.0 mm (2% of scans) with 93% of scans taken at 1.25 mm spacing or lower. 47 subjects with rib fractures were retained in the study, however subjects with extreme skeletal abnormalities or fixation devices present in the scan were excluded.

Costal Cartilage Identification
To identify regions of costal cartilage calcification from within the CT image volumes a set of curved 3D reformations through those image spaces were developed via custom-made routines in MATLAB 2016b (The Mathworks Inc., Natick, MA). These reformations serve to spatially isolate the anterior chest wall (containing the costal cartilage segments and the sternum) from other parts of the body. Within this space, traditional histogram-based segmentation and morphological operations can then extract the volumetric regions of locally calcified cartilage.

The reformations are based on a grid of landmarks that are placed manually into the 3D space of the CT scan at (1) the ends of left and right ribs (designating the start of each costal segment), (2) the sternal connection locations (or ends of each costal segment), and (3) a point approximately mid-way along each costal segment at its cross-sectional centre. A curved 3D surface is then generated that passes smoothly through this grid of landmarks [16], forming an approximate representation of the mid-surface of the anterior chest wall as depicted in Fig. 1 (left). A volumetric region encompassing the costal cartilage is identified as the 3D space within a 10 mm offset from this mid-surface. Anatomically, costal cartilage segments meet the ribs at a cup-shaped depression in the rib cortical bone, and the rib end landmark is placed specifically at the apex of this cup [4]. Similarly, a depression is present at the sternal end of the cartilage segments and the apex of each cup is chosen for the placement of each sternal connection landmark. To ensure accuracy, custom MATLAB interfaces were written allowing a user to place an approximate landmark on regular axial CT slices, then adjust that landmark using multiply resliced oblique views centred on that local region.

Image voxels for the 2nd through 5th rib cartilage segments were resampled through this curved volumetric region from the original CT data using bilinear interpolation. The zone between each sternal landmark was excluded, and the remaining space was partitioned into individual segments for each rib level based on proximity to the central curve from each rib end to sternal connection point. A threshold of 180 Hounsfield Units (HU) was used to separate calcified regions of cartilage from the other (lower density) surrounding tissues. Minor morphological operations then removed extremely small calcification regions (less than 1 mm3) and to remove the internal thoracic arteries which run vertically adjacent to the sternum, producing the isolated regions of calcification as illustrated in Fig. 1 (right). Note that under this overall segmentation scheme the small amount of bone contiguous with the rib or the sternum which forms the connecting cup (which is on the order of 5 mm deep) will also be classified as calcification.
Fig. 1. Example mid-surface of the chest wall through cartilage segments built from the grid of manually placed rib end, sternum connection, and mid-segment land marks (left). In this view costal cartilage calcification is clearly visible as white regions along segments. Full volumetric regions from the same subject are shown in 3D (right).

**Measured Variables and Statistical Analyses**

The primary object of measurement was the volumetric amount of calcification identified within each cartilage segment space, and this volume, $V$, was recorded for each segment in units of mm$^3$. To improve data normality for statistical analyses, and to retain conceptual understanding, volumetric results are presented in this study by a cubed root transformation to the edge length $E$ (mm) of a cube containing the equivalent volume of calcification as was measured from within the costal segment. A secondary measurement for the extent of calcification along a segment was characterised by the lengthwise percentage ($\text{LenPcnt}$, %) of each costal segment that contained any calcified region within its cross section. For example, a segment with calcification regions emanating from the ribs and from the sternum each involving some portion of 20% of the segment’s overall length would be designated with a lengthwise percentage ($\text{LenPcnt}$) of 40%.

These measurements were taken from eight separate cartilage segments (ribs 2 through 5, left and right sides of the body), amounting to a total of 1640 observations. Results are reported firstly on a per-segment basis and, for statistical analyses, the average $E$ and $\text{LenPcnt}$ values are taken across all segments per individual reducing the data to one observation per individual. Multivariable linear regression is performed to investigate associations between measured variables and subject age and sex, with statistical significance reported at the $p<0.05$ level.

**III. RESULTS**

Measurements of calcification volume were collected from all costal cartilage segments. Fig. 2 shows the population distribution of equivalent cube edge length ($E$, mm) of these volumes for males and females, stratified by rib segment level. These distributions show that males typically have a higher calcification volume than females at each segment level ($p<0.01$). Lower rib levels (4 and 5) are also seen to contain a marginally greater volume of calcification than levels 2 and 3 (with $E$ increased by 2.1 mm, $p<0.01$). For reference, the average segment lengths are given in Fig. 2, showing a clear trend for lower cartilage segments being longer than upper segments at increments of approximately 8 mm. When considering the percentage length of rib segments that show calcification involvement ($\text{LenPcnt}$), there are no longer clear sex differences or differences in extent calcification by rib segment level.
Fig. 2. Results per segment for the overall calcification volume (given by the equivalent cube edge length, $E$), the geometric length of each segment (mm), and the percentage length of a cartilage segment with non-zero calcification involvement ($LenPcnt$). Boxes show the median and the 25th to 75th quantile ranges and whiskers extend to the ±2.7 sigma range (99.7% coverage).

The measurements of calcification volume ($E$) were averaged across the eight costal segments for each individual, and are shown by age and sex in Fig. 3 below. Linear regression trend lines are also shown, with regression coefficients summarised in Table 1. Regression results showed significant increases ($p<0.0001$) in the volume calcification (with equivalent cube edge length, $E$, increasing at the rate of 0.9 mm per decade) and extent calcification with age (additional 6.9 % of segment length involvement per decade). Males had higher overall volumes of calcification (average $E$ across all segments being 1.56 mm larger, $p<0.0001$) than females, however no significant difference in extent calcification ($LenPcnt$) was seen between sexes ($p>0.1$). Results also did not support any sex-based differences in the rate of calcification accumulation with age, as subsequent regression models with an additional age-sex interaction term found that term to not be significantly different to zero ($p>0.1$).
Fig. 3. Average calcification volume (equivalent cube edge length, $E$) per segment by age (top left), and average lengthwise extent of calcified cartilage (LenPcnt, top right). Chest wall mid-surface images for individuals marked A-C are shown for comparison (bottom row).

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Estimate ($E$ (mm))</th>
<th>$r^2 = 0.35$</th>
<th>$p$</th>
<th>Estimate (LenPcnt (%))</th>
<th>$r^2 = 0.26$</th>
<th>$p$</th>
</tr>
</thead>
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<td>Intercept</td>
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<td></td>
<td>21.805</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>Sex (0=M, 1=F)</td>
<td>-1.567</td>
<td>&lt; 0.0001</td>
<td></td>
<td>-5.502</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.089</td>
<td>&lt; 0.0001</td>
<td></td>
<td>0.689</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
</tbody>
</table>

IV. DISCUSSION

This study reports quantitative measurements of costal cartilage calcification taken from CT images from a population of live adult subjects. There has been previous in-depth quantitative analysis of cartilage segments from 11 PMHSs at the microstructure level using MicroCT [4], and limited quantitative data from analysis of large populations for the purpose of age and sex determination using X-ray imaging [9,10]. The measurements presented here are intended to assist researchers design calcification schemes that can be added to current human body computational models in order to better model the aging process within the costal cartilage.

In part due to a limited amount of available information, current thoracic computational models assign a single homogeneous material to the costal cartilage, with material properties representative of the hyaline cartilage mid-substance without calcification [17-19]. Such finite element models, however, have the capacity to assign specific material properties to individual finite elements within a solidly meshed part. Furthermore, shell elements can be added to cartilage surface parts to form a separate perichondrium layer, again capable of non-uniform material properties.

Forman and Kent [20] implemented an inhomogeneous cartilage material into subject-specific finite element component models of the costal cartilage. Their modelling schematic included setting the distinct solid finite elements corresponding to regions of calcification (as derived from CT images of the cadaveric specimens being modelled) to a stiffer material property. Forman and Kent [15] further expanded this methodology by introducing a parametric calcification severity, whereby progressively larger (or smaller) clusters of elements were assigned the calcification material model compared to a baseline individual. The calcification scoring system used was based partly on methods developed by McCormick [7] from anterior X-ray images. The
technique used here instead utilises 3D volumetric data from CT images to quantify calcification amounts. This could advance the modelling methodology (whereby specific finite elements are set to a calcified material property) by setting volumetric targets explicating the amount that a calcification region should expand in order to provide a target volume of calcification and consequently represent a chosen increase in age.

Microstructural studies have shown that calcification can occur in multiple different structured morphologies including, in some cases, dense shells surrounding a core of struts similar to trabeculae [4]. While not possible to discern under clinical CT scan resolutions, these fine details are also not easily represented in current full body computational models (which have cartilage element edge lengths in the order of 2-10 mm). This study has consequently focused on quantifying the overall volumes of calcification within a segment and understanding a simplified representation of its spatial distribution. Analytic work has explored microstructural connectivity variations in cartilage, simulating the elastic modulus of heterogeneous cartilage segments with calcified regions assigned either in clusters or dispersed throughout a cartilage segment [21]. Results showed that stiffness increases substantially as calcification connectivity increases, suggesting that FE models would exhibit different behaviour based both on the amount of calcification imposed, and on its spatial configuration within a cartilage segment.

The volumes of calcification reported in the current results are consistent with expectations based on previous literature. Most studies report that calcification typically begins to form in approximately the third decade of life [9,22], is commonly of moderate severity between ages 50–60 [5,7], and is moderate or severe in approximately 45% of persons over 75 [7,23]. The current data largely reflects these trends, however it is notable that the lowest end of the calcification volume distribution does not actually reach zero. This is likely due to the relatively simplistic delineation between rib bone and costal cartilage that is used here, whereby the cartilage and rib or sternal bones are separated via an assumption about their connections’ cup-shaped morphology. This assumption means that the periphery of this cup-shaped depression likely contains small volumes of rib bone which are being considered as calcified volume, making the overall calcification volume non-zero.

Observation of the calcification patterns seen from mid-surface reformations of the chest wall (see Fig. 3 second row, for example) match well with previous descriptions of sex-based differences in the morphology of accumulated calcified cartilage. Specifically, males are reported to exhibit a peripheral pattern characterised by ossification of the inferior and superior costal cartilage margin, whereas females show one or more central calcification patterns with pyramidal-shaped central tongues of ossification or centrally-placed smooth globules of ossification [6,22]. Such differences are seen clearly in the two highly calcified individuals highlighted in Fig. 3 (lower row), and similar patterns were observed across most other individuals. Cartilage calcification occurs as calcium uptake into the cartilage tissue increases. The underlying mechanism for this difference between males and females in costal cartilage calcification patterns has not been fully explored. However, with calcium uptake into cartilage tissue being the primary cause of calcification in general, early hypotheses have come from finding similar dimorphisms in cartilage presentation near the thyroid gland suggesting hormonal differences between males and females may be involved [6,24,25], as well finding high calcium concentrations in sections of the aorta more frequently in males than females [25].

In terms of its application to computational models, one limitation of the data presented here comes from the fact that it is based on the segmentation of calcified regions of the costal cartilage, but without an accompanying segmentation of the overall cartilage segment. The reason for this is that the difference in radiodensity between costal cartilage and its various surrounding tissues (such as muscle, fat) is relatively small, such that a simple histogram-based threshold is unable to clearly separate these body components. Cartilage calcification, on the other hand, is considerably denser than other local materials and as such it can be easily segmented after localising the containing region for a given segment of costal cartilage. The consequence of measuring only the calcified regions within a segment is that no true volumetric percentage of calcification can be reported. As a surrogate for this more desirable measurement, we have utilised the costal segment length (which does not require segmentation of a full cartilage segment) and chosen to report a lengthwise percentage of calcification as a guide for researchers choosing a scheme for calcification growth along the cartilage segment.
V. CONCLUSIONS
Measurements of costal cartilage calcification volumes and distribution have shown significant trends with age. Age and sex are seen to account for around 35% of all inter-individual population variability in the total volume of calcified cartilage. The lengthwise extent of calcified regions of a cartilage segment is also seen to increase significantly with age. Results provide volumetric guidelines for the introduction of regional calcification within the costal cartilage. Specifically, it is recommended when incorporating person-age into models that the calcified cartilage volume should increase at the rate of 0.9 mm (for an equivalent cube edge length) per decade, and should involve an increasing lengthwise extent of the cartilage segment at a rate of at least 7% per decade.

VI. REFERENCES

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