# Assessment of healthy trapeziometacarpal cartilage properties using indentation testing and contrast-enhanced computed tomography.

Running Head: Assessment of TMC cartilage properties

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## Abstract

*Background:* The trapeziometacarpal joint is a common site for osteoarthritis development in the hand. When osteoarthritis is present, it results in significant functional disabilities due to the broad range of activities performed by this joint. However, our understanding of osteoarthritis initiation and progression at this joint is limited because of the current lack of knowledge regarding the properties and structure of the corresponding cartilage layers. The objective of this study is to assess the morphological and mechanical properties of trapeziometacarpal cartilage via the combination of indentation testing and contrast-enhanced computed tomography. Such research may lead to the development of medical imaging-based approaches to measure cartilage properties *in vivo*.

*Methods:* Intact first metacarpals and trapezia were extracted from 16 fresh-frozen human cadaver hands. For each specimen, load-displacement behavior was measured at 9 testing sites using a standardized indentation testing device to calculate the normal force and Young's modulus of the cartilage sub-regions. The specimens were then immersed in CA4+ contrast agent solution for 48 hours and subsequently scanned with a resolution of 41μm in a HR-pQCT scanner to measure cartilage thickness and attenuation. Finally, correlations between compressive Young's modulus and contrast-enhanced computed tomography attenuation of the cartilage were assessed.

*Findings:* No significant difference was found in cartilage thickness between the trapezium and first metacarpal, but the comparison between articular regions showed thinner cartilage around the volar aspect of both the first metacarpal and the trapezium. The first metacarpal cartilage was stiffer than the trapezial cartilage. A significant positive correlation was observed between Young's modulus and mean contrast-enhanced CT attenuations in superficial and full-depth cartilage in both the first metacarpal and the trapezium cartilage.

*Interpretation:* The quantitative measurements of trapeziometacarpal thickness and stiffness as well as a correlation between Young's modulus and contrast-enhanced computed tomography attenuation provides a method for the non-destructive *in vivo* assessment of cartilage properties, a greater understanding of thumb cartilage behavior, and a dataset for the development of more accurate computer models.

**Keywords:** Thumb, trapeziometacarpal joint, cartilage properties, contrast-enhanced computed tomography, osteoarthritis

## 1. Introduction

Osteoarthritis (OA) is one of the most prevalent joint diseases and represents a leading cause of disability for millions of people around the globe ([Royal College of Physicians], 2008; Cisternas et al., 2016). OA is multifactorial condition that can originate from a diversity of factors, including genetic, physiological and mechanical prevalence (Brandt et al., 2009; Felson, 2000; Fontana et al., 2007; Hunter and Wilson, 2009; Wilson et al., 2008). It is also categorized as a degenerative joint disease due to its biochemical and morphological impact on articular cartilage (Cisternas et al., 2016). The primary function of cartilage is to provide joints with a low-friction gliding surface which distributes loads and allows smooth joint motion (Buckwalter et al., 2005). However, when OA occurs, the cartilage progressively degenerates increasing the contact pressure and leading to adverse morphological changes (D'Agostino et al., 2017). The most common symptoms of OA are articular pain and progressive loss of normal joint function (Woolf and Pfleger, 2010). OA is also strongly associated with aging (Hinton R, Moody RL, Davis AW, 2002; Petersson, 1996) and its prevalence is expected to increase in the upcoming decades due to increasing life expectancy (Hootman et al., 2016). However, despite its significant societal burden, limited information is known regarding the initiation and

progression of OA as well the relationships between biomechanical properties and tissue composition for specific tissues prone to develop OA, such as those found in the hand.

The trapeziometacarpal (TMC) joint is a common site for OA development, with about 30% of post-menopausal women and 8% of men developing radiological signs of TMC OA (Armstrong et al., 1994). In comparison, the Arthritis Foundation estimates that half of the US adult population develops symptoms of knee OA during their lives and that 25% develop symptoms of hip OA by the age of 85. The TMC is also an important joint to hand function that has not received enough attention in the last decades in comparison with other joints. It constitutes the base of our opposable thumb and enables the hand to grip, grasp and perform precision tasks (Edmunds, 2011; Koff et al., 2003; Tsai and Beredjiklian, 2008). With the recent development of new technologies (e.g. smartphones, tablets), the human thumb is currently undergoing new cycles of stress and strain that require more attention to better understand its behavior and prevent the development of degenerative thumb conditions. For instance, TMC OA is thought to be caused by abnormal joint mechanics and is known to significantly affect hand function and quality of life ([Royal College of Physicians], 2008).

One approach for understanding the role of mechanics in the development and treatment of OA is to develop accurate joint models based on the biomechanical behavior of each structure (Dourthe et al., 2016). Such methods require exact information about the anatomy and mechanical properties of each articular component, including the articular cartilage. Several studies have been performed to either assess the dimensional (Afara et al., 2013; Koff et al., 2003; Varga et al., 2013) or mechanical (Bansal et al., 2010; Barker and Seedhom, 2001; Lakin et al., 2015, 2013) properties of animal and human cartilage at different joints, and showed that such properties are species-, joint-, and sometimes, bone-specific (Varga et al., 2013). However, to our knowledge, no study has yet evaluated the mechanical properties of cartilage in human TMC joints.

One of the main challenges regarding the measurement of cartilage properties is that most approaches are based on compression (confined, unconfined) or indentation testing, which are highly invasive and therefore, only applicable *in vitro*. However, the recent progresses in medical imaging technologies are leading toward the development of new methodologies which aim to enable the non-destructive assessment of subject-specific cartilage properties (Lakin et al., 2017; Lusic and Greenstaff, 2014).

More specifically, Contrast-Enhanced Computed Tomography (CECT) is an imaging method used for quantification of glycosaminoglycan (GAG) content of cartilage. Recently, a novel cationic contrast agent (CA4+), which is attracted to negatively-charged GAG molecules, has been developed for use in CECT (Bansal et al., 2011; Lakin et al., 2013). The accumulation of this contrast agent in cartilage is reflected on X-ray attenuation in CECT images and is directly proportional to the GAG content. The contrast agent (CA4+) has a higher sensitivity to GAG content than its anionic counterparts (Bansal et al., 2011; Lakin et al., 2014). GAG loss, an early indicator of OA (Felson, 2000), is associated with reduced cartilage compressive stiffness (Lakin et al., 2016). The association between CECT attenuation and cartilage stiffness has been established in animal cartilage plugs (Bansal et al., 2011; Lakin et al., 2014, 2016, 2013), human metacarpal cartilage (Lakin et al., 2015), and intact human knee cartilage (Stewart et al., 2017), but the association between CECT attenuation and cartilage stiffness in intact TMC cartilage has not yet been defined.

The rationale for this research is to determine the correlation between the CECT attenuation and mechanical properties of TMC cartilage, ultimately contributing to the development of a CECT-based technique for the *in vivo* assessment of cartilage properties. More specifically, the objectives of this study are: (1) to measure the thickness and compressive stiffness of TMC joint cartilage, (2) to describe how thickness and compressive stiffness are distributed across each articular facet, and (3) to evaluate the association between CECT

attenuation and cartilage compressive stiffness in TMC joint cartilage. Considering the potential clinical *in vivo* applications of CECT imaging, such association may improve our understanding of cartilage behavior and lead to more performant OA detection methods.

## 2. Methods

### *2.1.Specimen preparation*

The trapeziometacarpal (TMC) joint (i.e. first metacarpal, trapezium and intact joint capsule) of 16 fresh-frozen cadaveric hands (10 female, 6 males, age: 66-101 years, 15 right, 1 left) was excised by an orthopaedic hand surgeon (PDA) at the Jan Palfijn Anatomy Lab (University of Leuven, Kortrijk, Belgium). After harvest, each specimen was visually inspected by an orthopaedic hand surgeon (PDA) for cartilage degeneration or eburnation before being stored in a freezer at a temperature of -20°C. Any specimen showing advanced eburnation of the cartilage was not considered in this study (> Eaton stage II (Eaton et al., 1984; Eaton and Glickel, 1987)). Once the 16 specimens were collected, each specimen was sealed in a container filled with phosphate-buffered saline (PBS) solution to maintain the integrity of the specimens during transfer (where a temperature of -20°C could not be maintained). The specimens were shipped to the Centre for Hip Health and Mobility (Vancouver, Canada), and stored at a temperature of -20°C prior to testing and imaging. Approval from the appropriate Ethics Boards of the Faculties of Medicine of the University of Leuven, Belgium (number NH019 2016-09-01) and the University of British Columbia, Vancouver, Canada (number H16-01593) was obtained prior to the start of this study.

### *2.2.Cartilage indentation testing*

Specimens were thawed for 24h at room temperature prior to testing. Subsequently, the TMC joint capsule was opened to separate the first metacarpal (MC1) from the trapezium and

soft tissues were carefully removed around the TMC articulating surfaces. Seven testing sets were created by fixing 4-6 samples in a container using rigid foam (FOAM-iT!® 26, Smooth-On, Inc., Macungie, PA, USA). After solidification of the foam (**Fig. 1A**), each set was mounted in the indentation chamber (**Fig. 1B**) and immersed in PBS to keep the cartilage hydrated while testing (**Fig. 1C**).

For each sample (i.e. 16 MC1 and 16 trapezia), nine testing locations were manually selected across the TMC articular surface corresponding to nine anatomical sub-regions, as defined in previous reports (D'Agostino et al., 2017; Dourthe et al., 2016). Force-displacement behavior of the cartilage at each testing location (i.e. 'sub-region') was assessed using an indentation testing device (Mach 1, Biomomentum Inc, Laval, Quebec, Canada) with a spherical indenter (1 mm diameter). The major advantage of this device is that it enables a normal indentation of the cartilage (independently of its orientation) by calculating its surface orientation at each testing location using the coordinates of 4 points located at a distance of 1 mm from the point tested. Indentation parameters were kept constant for each sample (depth: 0.1 mm, velocity: 0.5 mm/s, relaxation time: 10 s). The indentation depth was chosen to enable a total indentation representing 10-20% of the total thickness of the cartilage. Koff et al. (Koff et al., 2003) reported an average thickness of 0.7 mm and 0.8 mm for MC1 and trapezial cartilage respectively. Therefore, we decided to fix the indentation depth at 0.1 mm. This displacement amplitude was also selected to keep the stress on the cartilage within a physiological range (2-11 MPa) and prevents cartilage damage (Clements et al., 2001) (stress calculation was based on Hertz equation). The indentation velocity was chosen to ensure an elastic response of the cartilage (Samosky, 2002; Samosky et al., 2005) and the relaxation time was set to observe initial relaxation of the cartilage after indentation. The peak normal force was recorded and the Young's modulus (E) was calculated at each testing location using an elastic model based on the corresponding force-displacement data and cartilage thickness

196 measurement (Hayes et al., 1972). To provide a visual representation of how the Young's
197 modulus is distributed along the articular surface, color-maps were generated by interpolating
198 between the nine values calculated at each testing location.

199 *2.3.CECT imaging*

200 Prior to imaging, each set of samples was immersed in a cationic contrast-agent solution
201 (CA4+, concentration of 12 mg of iodine/mL) mixed with protease inhibitors for 48h to allow
202 complete diffusion of the contrast agent into the cartilage (Bansal et al., 2010). CT images were
203 acquired using a High Resolution peripheral Quantitative Computed Tomography (HR-pQCT)
204 scanner (Xtreme CT, Scanco Medical, Zurich, Switzerland) with an isotropic voxel resolution
205 of 41μm (300 μA, 120 kV, maximal resolution provided by the HR-pQCT).

206 *2.4.Cartilage segmentation, thickness and attenuation*

207 The cartilage was segmented from the subchondral bone using a threshold-based
208 algorithm combined with manual segmentation. More specifically, sample-specific thresholds
209 were defined to facilitate the separation between cartilage and subchondral bone, and manual
210 segmentation was applied to correct for potential irregularities (based on the estimated
211 geometry of the TMC joint and its cartilage layers). To facilitate the visual identification of
212 each indentation test site, a 3D model of each set of samples was generated from the HR-pQCT
213 images (in the same coordinate system as the one used by the camera registration system) using
214 a commercially available medical imaging processing software (Mimics Research 18.0 x64,
215 Materialise, Leuven, Belgium) and oriented according to the top-view provided by the camera
216 registration system (**Fig. 2**). Cartilage thickness was measured for each indentation test location
217 on the 2D DICOM images as the distance between the test location on the surface of the
218 cartilage and the subchondral bone, perpendicularly to the subchondral bone edge (**Fig. 2**). To
219 provide a visual representation of how the thickness is distributed along the articular surface,

color-maps were generated by interpolating between the nine values measured at each testing location.

Considering that the indentation was performed on the superficial cartilage, we calculated the mean CECT attenuation for the entire segmented cartilage (full depth, **Fig. 3B**) and for the superficial cartilage layer (0.2 mm depth – **Fig. 3C**) independently (in Hounsfield Units (HU)). To ensure an accurate separation between cartilage and subchondral bone, the outcome of each segmentation was visually inspected and approved based on the known morphology of the TMC joint and its cartilage structure.

### *2.5.Statistical analysis*

Statistical tests were performed using R ("R Core Team. R: A language and environment for statistical computing.," 2013), with an alpha level of 0.05. The normality of the data was confirmed using a Shapiro-Wilk test. To ensure that the analysis was confined to the articular cartilage, test locations where the indenter did not get in contact with the cartilage were considered as outliers and excluded from the analysis. These outliers corresponded to either (1) articular sub-regions where total cartilage eburnation was observed (i.e. no cartilage observed on the CECT image at the corresponding location, leading to a thickness measurement of zero) or (2) edge zones where the indenter hit remains of the joint capsule (i.e. white zones on **Fig. 2**, very soft, leading to a peak normal force and Young's modulus close to zero). The differences between the MC1 and trapezium were tested using a Student t-test (Welch two sample t-test, one- or two-sided, unequal variances).

The effect of articular sub-regions on the peak normal force, Young's modulus and thickness was tested using a one-way ANOVAs (dataset without outliers), for both the MC1 and trapezium. A post-hoc test (Tukey's Honest Significant Difference test) was performed to assess the levels of differences between the three articular regions defined as *dorsal* (mean of

the dorsal-radial, dorsal-central and dorsal-ulnar sub-regions), *central* (mean of the central-radial, central and central-ulnar sub-regions) and *volar* (mean of the volar-radial, volar-central and volar-ulnar sub-regions). The decision to run this analysis on three articular regions instead of all nine articular sub-regions was taken based on the lack of statistical differences observed between the corresponding groups of sub-regions (e.g. no statistical difference when isolating the data from the central-radial, central and central-ulnar sub-region - Fig. 5) and to simplify the interpretation of the results (i.e. decrease the large amount of comparisons for the post-hoc test). To account for type 1 error rate in the context of post-hoc analysis, a family-wise alpha (FWα) of 0.14 was calculated using the following formula:

$$FW\alpha = 1 - (1 - \alpha_{IT})^{c}$$

Where:

$\alpha_{IT}$ = alpha level for an individual test (e.g. 0.05)

c = Number of comparisons

Finally, we examined the correlation between mean Young's modulus and mean CECT attenuation averaged over full-depth and surface cartilage among all MC1 and trapezium samples. We did so by calculating the Pearson correlation coefficient, with a value between 0.3 and 0.6 indicating a moderate correlation, and any value above 0.6 indicating a strong correlation.

## 3. Results

### *3.1. Cartilage Young's modulus and thickness analysis*

The peak normal force and Young's modulus were significantly higher ($P = 0.0002$ and $P = 0.002$ respectively) for the MC1 (peak normal force: mean 0.12 (SD 0.13) N; Young's

modulus: mean 1.64 (SD 1.86) MPa) than the trapezium cartilage (peak normal force: mean 0.07 (SD 0.08) N; Young's modulus: mean 0.99 (SD 1.26) MPa) (**Fig. 4A-B**). No statistical differences in thickness were found ($P = 0.8$) between the MC1 (mean 0.60 (SD 0.29) mm) and trapezium cartilage (mean 0.61 (SD 0.42 mm)) (**Fig. 4C**). In addition, no correlation was found between cartilage mechanical properties (i.e. peak normal force and Young's modulus) and cartilage thickness.

### *3.2.Analysis of articular regions and sub-regions*

For both MC1 and trapezium cartilage, no significant differences were found among the nine articular sub-regions for peak normal force (MC1: $P = 0.27$; Trapezium: $P = 0.92$) and Young's modulus (MC1: $P = 0.99$; Trapezium: $P = 0.86$) (**Fig. 5A-B**).

For cartilage thickness, the statistical difference between the nine articular sub-regions was significant for both the MC1 ($P < 0.0001$) and trapezium cartilage ($P = 0.0001$) (**Fig. 5C**). When looking at the three articular regions, the post-hoc analysis showed that the dorsal region was significantly thicker than the central (MC1: $P = 0.06$; Trapezium: $P = 0.01$) and volar region (MC1 and Trapezium: $P < 0.0001$). In addition, the volar region was significantly thinner than the central region (MC1: $P < 0.0001$; Trapezium: $P = 0.04$) (**Fig. 5C**).

### *3.3.CECT attenuation*

The two attenuations measured were smaller for the trapezium than for the MC1 ($P < 0.01$), with mean 1,949 HU (SD 334) (range: 1,500-2,700) and mean 1,204 HU (SD 132) (range: 1,000-1,450) for the full-depth and superficial trapezial cartilage, and with mean 2,180 HU (SD 398) (range: 1,500-2,850) and mean 1,411 (SD 239) (range: 1,000-1,900) for the full-depth and superficial MC1 cartilage respectively. CECT attenuation increased from superficial to deep cartilage, both for the MC1 and the trapezial samples (**Fig. 6**).

290 Similar patterns were observed when comparing the color maps representing the
291 distribution of Young's modulus and CECT attenuation for each individual subject (**Fig. 7**).

292 The correlation coefficients ($R^2$) between Young's modulus and average CECT
293 attenuation were all positive, with 0.62 (full-depth) and 0.68 (superficial) for the MC1 samples,
294 and 0.59 (full-depth) and 0.65 (superficial) for the trapezial samples (**Fig. 8**).

295

296 ## 4. Discussion

297 To facilitate the study of OA initiation and progression in the thumb, we assessed the
298 distribution of cartilage thickness and Young's modulus in TMC joint specimens and evaluated
299 the correlation between CECT attenuation and cartilage stiffness. The MC1 cartilage was stiffer
300 than the trapezial cartilage, but there was no difference in cartilage thickness between the two
301 sides of the joint. For both the trapezium and MC1, there was no significant difference in
302 cartilage Young's modulus between articular sub-regions. However, cartilage thickness
303 decreased from dorsal to central to volar. Finally, a significant correlation was observed
304 between CECT attenuation and cartilage stiffness for the MC1 and trapezium.

305 Our findings for cartilage Young's modulus are in the range reported for other joints
306 (Bansal et al., 2010; Barker and Seedhom, 2001; Buckwalter et al., 2005; Lakin et al., 2015),
307 with a mean of 1.64 (SD 1.86) MPa and a peak value at 9.44 MPa for the MC1, and a mean of
308 0.99 (SD 1.26) MPa and a peak value at 7.35 MPa for the trapezium. These values are higher
309 than the range of 0.4 to 4.2 MPa reported for the head of the fourth metacarpal by Lakin et al.
310 (Lakin et al., 2015). This might be due to the difference in study design, as our tests were
311 performed at nine distinct test locations, whereas Lakin et al. (Lakin et al., 2015) only tested a
312 single location per sample. It is also hypothesised that this difference results from higher
313 mechanical demands of the TMC joint compared with the fourth metacarpophalangeal joint. To

314 our knowledge, there are no data on the Young's moduli of the cartilage of other
315 metacarpophalangeal or carpometacarpal joints which hinders a broader comparison.

316 We also observed a significant difference between the compressive modulus of the MC1
317 and trapezium documenting that cartilage properties can differ between the two opposing facets
318 of a single joint. Assuming a correlation between intra-articular pressure and cartilage
319 degeneration, a lower compressive modulus for the cartilage layer of the trapezium could imply
320 a higher risk of cartilage eburnation at the trapezial facet, as reported by Pellegrini (Pelligrini,
321 1991).

322 Our results for cartilage thickness are consistent with previous work. The mean
323 thicknesses reported here (i.e., 0.60 mm for the MC1 and 0.61 mm for the trapezium) are
324 comparable to, though slightly thinner, than the measurements made using photogrammetry
325 (Koff et al., 2003) (i.e. mean 0.7 (SD 0.2) mm for the MC1 and mean 0.8 (SD 0.2) mm for the
326 trapezium). These authors also reported a significant decrease in trapezial cartilage thickness
327 between stage IV and stage I OA, but for the MC1, no significant differences in cartilage
328 thickness were reported between OA stages.

329 Our finding that the cartilage layers of the MC1 and trapezium are significantly thinner
330 on the volar side may help explain observed patterns of cartilage degeneration in TMC OA.
331 Several studies have reported that contact occurs around the volar side when the thumb is in a
332 neutral posture (Ateshian et al., 1995; D'Agostino et al., 2017; Dourthe et al., 2016; Halilaj et
333 al., 2015), as well as during lateral pinch (Ateshian et al., 1995; D'Agostino et al., 2017;
334 Dourthe et al., 2016; Goto et al., 2014; Kuo et al., 2014; Pellegrini et al., 1993), abduction
335 (Ateshian et al., 1995; D'Agostino et al., 2017; Goto et al., 2014; Halilaj et al., 2015), adduction
336 (D'Agostino et al., 2017; Halilaj et al., 2015), and flexion (Ateshian et al., 1995; D'Agostino et
337 al., 2017; Halilaj et al., 2015). The fact that contact seems to mostly occur in areas of thin

cartilage (i.e. where cartilage might have a decreased ability to withstand compressive loading) might facilitate the development of OA in these specific regions.

We found a significant correlation between compressive Young's modulus and CECT attenuation in both MC1 and trapezial cartilage samples, which is consistent with previous studies performed on animal cartilage plugs (Lakin et al., 2014, 2013) and human third-metacarpal cartilage (Lakin et al., 2015). The stronger correlation observed between superficial CECT attenuation and compressive Young's modulus (compared to full thickness CECT vs Young's modulus) is consistent with previous findings and explained by the higher relative contribution of GAGs to cartilage stiffness in the superficial region (Samosky, 2002; Samosky et al., 2005). The correlation coefficients determined in this study are slightly lower than the ones reported by Lakin et al. (Lakin et al., 2015) for MC4 cartilage. This is likely explained by differences in composition and biomechanical behavior of the tested samples and in the indentation protocol (one testing location vs. nine). Our observations of depth-dependant CECT attenuation patterns are consistent with those reported by Lakin et al. (Lakin et al., 2015) and in several other recent investigations (Bansal et al., 2011; Lakin et al., 2014, 2016, 2013). This indicates that CECT with CA4+ has the potential to become an applicable method for the non-destructive assessment of cartilage properties. Being able to measure cartilage properties of specific joint sites in OA patients at different stages of the disease would be a major progress in OA diagnosis and research.

A key strength of this study is that both imaging and mechanical testing were performed on intact articular surfaces, which more accurately represents the physiological behavior of the joint than excised cartilage plugs. Considering the destructive nature of histology and the invasive nature of indentation testing, CECT remains a promising alternative for subject-specific cartilage assessment, and potentially for bone assessment as well. A key limitation of the study was the exclusion of some cartilage sub-regions due to advanced cartilage

363 degeneration. Due to the nature of the tests, this study was performed on cadaveric specimens
364 coming from donors above the age of 60. As a result of the high prevalence of OA in the elderly
365 population (Hinton R, Moody RL, Davis AW, 2002; Petersson, 1996), some of these specimens
366 displayed zones of cartilage eburnation which led us to define an exclusion criterion (as defined
367 in the Methods). However, we excluded only points where there was evidence of total cartilage
368 eburnation (i.e. outliers). Zones of partial eburnation (i.e., cartilage still present but thinner than
369 the average healthy cartilage) could not be excluded considering the lack of evidence regarding
370 a potential thickness limit under which the cartilage could be considered as degenerated.

371 Another restraint is that, as a result of the *in vitro* aspect of the study, the potential
372 impact of handedness could also not be investigated, mostly because such information was not
373 available from the donors. Similarly, it should be acknowledged that the observed difference in
374 compressive modulus may be partially linked to the slightly different level of wear between the
375 MC1 and trapezium cartilage layers. This could potentially result from the original congruence
376 (or incongruity) of the joint. Ideally, a similar study should be done on samples obtained from
377 young and healthy individuals where joint congruence may not have yet impacted the integrity
378 of the joint. However, such investigation will only be possible if an accurate in vivo method
379 has been developed.

380 It should also be noted that this study only assessed the elastic properties of the cartilage
381 (i.e. compressive modulus). While full characterization of cartilage requires assessments of its
382 viscoelastic properties through approaches such as creep and stress relaxation tests, the time
383 required for these tests at each point would make mapping behaviour across the surface
384 challenging.

385 Finally, no histological assessment was performed to determine the exact relationship
386 between CECT attenuation and GAG content, although this relationship has been established

in previous studies (Bansal et al., 2010; Lakin et al., 2014). Additional research is ongoing to further evaluate the validity and clinical applicability of this method (e.g., larger sample sizes, histology assessment, tests regarding the potential use of the contrast agent *in vivo*).

## 5. Conclusion

In summary, this study provides quantitative assessment of TMC cartilage thickness and stiffness as well as a correlation between Young's modulus and CECT attenuation using the CA4+ contrast agent. These findings improve our understanding of cartilage TMC mechanics as well as provide insight for the development of more accurate cartilage models in the future. It also illustrates the potential applications of CECT imaging for the non-destructive assessment of cartilage properties, which will ultimately facilitate early detection of OA in the TMC joint and lead toward more efficient diagnosis and treatment strategies.

## 6. Conflict of interest statement

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

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