Computed Tomography–Mediated Registration of Trapeziometacarpal Articular Cartilage Using Intraarticular Optical Coherence Tomography and Cryomicrotome Imaging: A Cadaver Study

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Abstract
Objective. Accurate, high-resolution imaging of articular cartilage thickness is an important clinical challenge in patients with osteoarthritis, especially in small joints. In this study, computed tomography (CT) mediated catheter-based optical coherence tomography (OCT) was utilized to create a digital reconstruction of the articular surface of the trapeziometacarpal (TMC) joint and to assess cartilage thickness in comparison to cryomicrotome data. Design. Using needle-based introduction of the OCT probe, the articular surface of the TMC joint of 5 cadaver wrists was scanned in different probe positions with matching CT scans to record the intrarticular probe trajectory. Subsequently and based on the acquired CT data, 3-dimensional realignment of the OCT data to the curved intrarticular trajectory was performed for all probe positions. The scanned TMC joints were processed using a cryomicrotome imaging system. Finally, cartilage thickness measurements between OCT and cryomicrotome data were compared. Results. Successful visualization of TMC articular cartilage was performed using OCT. The CT-mediated registration yielded a digital reconstruction of the articular surface on which thickness measurements could be performed. A near-perfect agreement between OCT and cryomicrotome thickness measurements was found ($r^2 = 0.989$). Conclusion. The proposed approach enables 3D reconstruction of the TMC articular surface with subsequent accurate cartilage thickness measurements, encouraging the development of intraarticular cartilage OCT for future (clinical) application.

Keywords
optical coherence tomography, articular cartilage, computed tomography, co-registration, imaging cryomicrotome

Introduction
Hand osteoarthritis (OA) is a major clinical problem, causing pain and disability to millions of patients worldwide. It is estimated that in a population of 55 years and older, up to 67% of women and 55% of men have radiographic signs of OA in at least one hand joint.1 The trapeziometacarpal (TMC) joint is the second most prevalent location of hand OA1 but may be a more important contributor to pain and impaired movement than OA of the interphalangeal joints.2 However, nearly half of patients with radiographic signs of hand OA have no clinical symptoms consistent with the diagnosis.3 Also, patients may have hand OA symptoms without radiological evidence to support the diagnosis. Agreement between hand surgeons and radiologists in staging TMC OA according to the Eaton-Littler classification4 is moderate at best.5 This important discrepancy between clinical signs and findings on imaging studies seems partly attributable to the quality of clinical cartilage imaging.

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The TMC is a complex joint in imaging of degenerative joint disease. Due to its saddle-shape, 2D analysis of degenerative characteristics on plain X-ray (joint space narrowing, formation of osteophytes) is difficult and unreliable in an early stage of the disease. Using (3D) computed tomography (CT), the cartilage itself cannot be depicted. Also, clinical magnetic resonance imaging lacks spatial resolution to accurately assess the thin cartilage layers that line the wrist joints. A promising technique in cartilage imaging is optical coherence tomography (OCT). OCT utilizes near-infrared light to nondestructively acquire high-resolution cross-sectional images of thin tissue layers. Applications of cartilage OCT have been demonstrated in animal studies and in vivo studies in large joints. Recently, our group showed the feasibility of fiber-optic, intraarticular, catheter-based OCT for in situ visualization of TMC articular cartilage in a pilot study. CT was used for co-registration of the intraarticular probe position during the experiment, enabling the reconstruction of a fused 2D image between OCT and CT. Histological slides of the imaged joint were produced for comparison of OCT and cryomicrotome processing. Since loss of articular cartilage thickness and quality are hallmark features in OA, accurate estimation of cartilage thickness would benefit staging of TMC OA greatly. Recent data show that using OCT, accurate cartilage thickness measurements of articular cartilage can be obtained. Previous studies have demonstrated that comparison of 2D OCT and histological slides is hampered by mismatches in localization and orientation between the images. Therefore, we hypothesize that 3D catheter-based OCT allows for highly accurate visualization of TMC articular cartilage thickness.

Utilizing a new approach, the goal of this study is to make an accurate comparison of OCT and cryomicrotome cartilage thickness measurements in 3-dimensionally corresponding areas of the TMC joint.

**Methods**

**Cadaver Specimens**

In this cadaver study, the ethical commission of the Amsterdam University Medical Centers waived the need for evaluation. Five fresh-frozen cadaver wrists, stored at −20°C, were used in this study. Forty-eight hours prior to the experiment, the wrists to be scanned were thawed at 4°C to allow for flexibility of the joints. None of the cadaver wrists had a known history of TMC OA and none had undergone previous TMC surgery.

**Optical Coherence Tomography**

A commercially available swept-source OCT system (Illumien, St. Jude Medical) was used, operating at a wavelength of 1300 nm with a bandwidth of 55 nm. The OCT system is interfaced to a 0.9-mm-thick fiber-optic OCT probe (C7-Dragonfly, St. Jude Medical). A typical OCT scan is performed in 5.4 seconds, producing a cylindrical 540-slice dataset with dimensions 10 × 10 × 540 mm and an axial and lateral resolution of 15 µm and 25 µm, respectively. Data were stored as Tiff stacks for further processing. Unprocessed OCT images are directly available for review on the console.

**Computed Tomography**

For registration purposes, CT was used to accurately depict the intraarticular position of the OCT probe during the experiment. On a 64-slice scanner (Brilliance 64, Philips), a clinical wrist scanning protocol was used with the following parameters: collimation 64 × 0.625, field of view 169 mm, slice thickness 0.67 mm, tube current 120 kV, 150 mA/slice exposure, image matrix 512 × 512 pixels.

**Experimental Procedure**

To approach the TMC joint, standard TMC arthroscopy portals were used. In short, the joint space was palpated and accessed through 2 portals: the first was placed volar to the adductor pollicis longus (APL) tendon, and the second was placed dorsal to the extensor pollicis brevis (EPB) tendon. The joint was accessed percutaneously using a standard 18-gauge IV cannula. After accessing the joint space, the needle was retracted to introduce the fiber-optic OCT probe through the cannula. The cannula remained in situ for intraarticular manipulation of the OCT probe and was retracted over the probe during OCT scanning to avoid artifacts in the OCT data. After each OCT scan, the probe remained in situ and subsequently a CT scan was acquired. Subsequently, the IV cannula was reinserted into the joint by sliding the cannula over the probe and repositioning the OCT probe to depict a different part of the articular surface. An OCT and a CT scan were made for 3 different intraarticular positions of the OCT probe in each cadaver specimen.

After all scans were completed, a 2 × 2 cm region of interest around the TMC joint location was marked on the skin using a permanent marker in anticipation of cryomicrotome processing.

**Cryomicrotome Processing**

Scanned wrists were refrozen at −80°C to allow for rigidity during sawing of the area containing the TMC joint. The TMC joint was extracted sawing along the lines of the previously marked region of interest using a band saw (Kolbe K430). TMC blocks were stored at −20°C until processed by the cryomicrotome system. Sectioning was performed using a custom-built cryomicrotome system equipped with high-resolution imaging capability, which was previously utilized.
for wrist cartilage measurements and ligament detection\textsuperscript{21,22} and had previously shown to be able to accurately determine small blood vessel diameters.\textsuperscript{23} The system consisted of an Apogee Alta U-16 imaging camera with 70 to 180 mm Nikon lens and illumination by a Power LED cluster (Luxeon V, Lumileds Lighting) fitted with corresponding imaging filters by Chroma Corp. After sectioning by the microtome, the digital camera takes images of the remaining sample surface, after which sectioning by the microtome is repeated until the entire sample is processed. Episcopic white light (excitation wavelength 440 nm, emission wavelength 505 nm) and cartilage autofluorescence (excitation wavelength 560 nm, emission wavelength 560 nm) images were obtained using the built-in filters. Using this system, a stack of 2D images was acquired and reconstructed into a high-resolution 3D dataset with $30 \times 30 \times 30 \mu m$ voxels.

**Image Reconstruction and Analysis**

For reconstruction, segmentation, and visualization, Amira visualization software was utilized (Version 5.4.1, FEI Visualization Sciences Group, Burlington, MA). OCT and cryomicrotome data dimensions were resized to arrive at voxel dimensions corresponding to those of the CT datasets. On CT, the TMC joint with intraarticular OCT probe was identified. Three CT datasets from the same sample representing 3 different intraarticular probe positions were loaded and built-in automatic (rigid) co-registration was performed. After alignment of the CT datasets, semiautomated, Hounsfield unit thresholded segmentation (HU $\geq 270$) of the trapezium bone (Trap) and the first metacarpal bone (MC1) was performed (Fig. 1).

Segmented voxels were reconstructed into a 3D surface mesh. In a similar way, the intraarticular OCT probe was segmented and reconstructed for 3 different probe positions, generating 3 different probe 3D mesh surfaces. A built-in centerline registration module was used to generate a CT-based centerline of the curved intraarticular trajectory of the OCT probe.

Subsequently, corresponding (rigid tube shaped) OCT datasets were loaded and reconstructed to 3D volumes (Fig. 2A). OCT datasets were prepared for 3D deformation to realign the OCT data to the curved intraarticular trajectory of the OCT probe as previously recorded using CT: OCT datasets were cut into 27-frame sections, starting with slice number 1 at the probe tip. Visual alignment of the rotatory component of the OCT data was performed using landmarks such as the articular surfaces and air bubbles seen on both OCT and CT. Thereafter, perpendicular manual realignment of the 27-slice sections onto the previously generated probe centerline was performed with preservation of rotatory position. Finally, the aligned 27-slice sections were merged creating a 3D realigned OCT dataset following the intraarticular probe trajectory (Fig. 2B). This process was repeated for all 3 probe positions and matching OCT datasets (Fig. 3).

Cryomicrotome data were visualized with semiautomatic, rigid co-registration of the cryomicrotome data and the TMC joint as seen on CT using Amira. Subsequently, the cryomicrotome data were used for segmentation of the thin cartilage layers on the trapezium and first metacarpal bone (Fig. 4). Segmented voxels were reconstructed into 3D meshes and projected onto the CT segmented Trap and MC1 articular surfaces (Fig. 5). Data reconstruction and visualization steps are schematically summarized in the flowchart in Figure 6.

**Measurements**

Following completion of 3D visualization, comparative measurements between OCT and cryomicrotome cartilage
thickness were performed by a single investigator. Thereto, cartilage thickness was measured for 5 different intraarticular positions in each OCT dataset and for each articular surface (Trap and MC1), amounting to 15 measurements per technique per articular surface. For all articular surfaces, an overlay of 3D OCT and cryomicrotome cartilage data was created (Fig. 7). Subsequently, random OCT thickness measurements were taken followed by a comparative cryomicrotome cartilage thickness measurement while measuring the same 3D position as much as possible by measuring on the same slice and in the same intraarticular location.

**Statistics**

Statistical computations were performed using GraphPad Prism 5 (GraphPad Software Inc, La Jolla, CA). Linear regression analysis (Pearson’s) was performed for comparison of
thickness measurements between OCT and cryomicrotome data.

**Results**

Three OCT datasets, each corresponding to a different intraarticular probe position, were acquired for each of the 5 cadaver samples. Successful visualization of cartilage surfaces was achieved on all acquired OCT datasets since the cartilage-bone interface could be identified clearly on OCT. Recombination of three 3D deformed OCT datasets yielded a reconstruction of the articular surfaces on the trapezium and first metacarpal (Fig. 3).

Cryomicrotome processing produced a high-resolution, 3D anatomic model of the imaged TMC joint in which cartilage layers could be segmented using the system’s auto-fluorescence channel (Figs. 4 and 5). Interestingly, the relative soft character of (postmortem) cartilage seemed prone to slight indentation by the OCT probe, as shown in Figure 7. Cartilage regions directly affected by probe indentation were excluded in subsequent measurements. The aforementioned indentations were not assessed on cryomicrotome images, suggesting a temporary effect of the OCT probe placement.

A total of 150 cartilage thickness measurements were acquired for both OCT and cryomicrotome data. Thickness measurements ranged from 0.29 to 1.09 mm for OCT and from 0.27 to 1.07 for the cryomicrotome data. Linear regression analysis to compare thickness measurements between OCT and cryomicrotome cartilage data showed a slope of 1.007 (95% confidence interval = 0.990-1.025) with a goodness-of-fit ($r^2$) of 0.989 (Fig. 8).

**Discussion**

This study is the first to report intraarticular OCT with co-registered CT in imaging of TMC articular cartilage for multiple intraarticular probe positions. The cryomicrotome system as reference yielded an accurate method for 3D cartilage thickness measurements and showed a near-perfect agreement between OCT and cryomicrotome imaging measurements.

Aforementioned measurement accuracy was facilitated by the creation of a 3D reconstruction of the TMC articular
surface, using co-registered CT data to realign the OCT slices to the intraarticular probe trajectory in 3D. However, manipulation of the probe (to create the different intraarticular positions) also produced small differences in position of the bone structures comprising the TMC joint (the trapezium and first metacarpal), resulting in small visual inaccuracies after co-registration of the CT data. Although great care was taken to minimize movement within the joint during probe manipulation, the aforementioned repositioning resulted in minute inaccuracies in the digital joint surface reconstruction based on the OCT data.

The rationale for using multiple probe positions was to scan a larger portion of the articular surface and attempt to create a digital reconstruction of the articular cartilage based on the cartilage data acquired in multiple OCT/CT scans. Standard arthroscopy portals were used to introduce the probe into the joint cavity. Given the very flexible nature of the fiber-optic OCT probe, probe positions differed slightly between specimens. In this study, 3 OCT scans were performed per specimen and co-registered with the same number of CT scans. In future studies, more than 3 OCT scans per joint may be acquired to depict an even larger portion of the joint surface. Thereto, visual repositioning of the probe during actual arthroscopy may assist in more systematically scanning the joint surface.

Compared to the pilot study, in which 2D histology slides were used as reference, the use of the 3D cryomicrotome system greatly facilitated matching between OCT and the reference standard since a direct overlay of OCT/CT and cryomicrotome/CT could be produced. Moreover, the setup chosen in this study enabled a very accurate comparison between OCT and cryomicrotome thickness measurements, with an $r^2$ of 0.989. Freeze-thaw cycles may influence optical and/or mechanical properties of articular cartilage; the probe indentation depicted in Figure 7 serves as an example to this observation. However, based on the measurement results and excluding the areas of indentation from thickness measurements, the authors have no reason to assume said freeze thaw influences affected the primary outcome measurements.

These results combined with earlier animal study data by our group show that 3D OCT is an accurate technique to measure cartilage thickness, which is an important attribute for clinical practice. A noteworthy disadvantage of intraarticular OCT is the fact that it remains a (minimally) invasive diagnostic procedure by introducing a needle. However, results of this study may aid the development of alternative high-resolution (noninvasive) imaging techniques such as high-field strength magnetic resonance imaging, which may provide an alternative reference standard to histopathology in the future.

As shown in the Methods section, numerous postprocessing steps were taken to create a digital cartilage surface reconstruction based on the 3D deformed OCT data. In coro-nary imaging, there have been reports on 3D deformation of OCT data based on angiographic studies, but to our knowledge, this is the first description of 3D deformed cartilage OCT data using co-registered CT. For clinical practice (a certain degree of) automation of these steps is needed to make intraarticular cartilage OCT a clinically feasible technique that can be used hands-on by the clinician, preferably in real time. Thereto, automation of the CT and 3D OCT co-registration process will be the subject of future studies.

Figure 8. Linear regression analysis of cartilage thickness measurements ($n = 150$), comparing OCT to cryomicrotome cartilage data.
Finally, this study was performed on cadaver material, which differs from in vivo cartilage in terms of rigidity and strength, demonstrated by the apparent indent of the OCT probe in the cartilage surface, as seen in Figure 6. In vivo tests are needed to be able to assess differences between cadaver cartilage and in vivo TMC cartilage more extensively.

Conclusion

This study demonstrates the use of 3D deformable, intraarticular OCT and co-registered CT in imaging of TMC articular cartilage and measurement of cartilage thickness. Scanning 3 different intraarticular probe positions per sample, a digital reconstruction of the scanned TMC articular surfaces could be produced, using CT probe position data to realign the OCT images in 3D. The use of a 3D cryomicrotome system enabled matching to OCT data and has therefore obvious advantages over 2D histopathology as a reference standard for thickness measurements. Thickness measurements between realigned cross-sectional OCT images and co-registered cryomicrotome cartilage data showed near-perfect agreement.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with authorship, and/or publication of this article.

Ethical Approval

In this cadaver study, the ethical commission of the Amsterdam University Medical Centers waived the need for evaluation.

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