Quantitative T2 mapping of the glenohumeral joint cartilage in asymptomatic shoulders and shoulders with increasing severity of rotator cuff pathology

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HIGHLIGHTS
• Glenohumeral cartilage T2 values were correlated to increasing rotator cuff pathology severity.
• Massive tear versus lesser injury differences were most evident in superior humeral cartilage.
• Sagittal T2 mapping best captures superior humeral head cartilage change in massive tear patients.

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ABSTRACT
Purpose: To examine the relationship between glenohumeral cartilage T2 mapping values and rotator cuff pathology.

Method: Fifty-nine subjects (age 48.2 ± 13.5 years, 15 asymptomatic volunteers and 10 tendinosis, 13 partial-thickness tear, 8 full-thickness tear, and 13 massive tear patients) underwent glenohumeral cartilage T2 mapping. The humeral head cartilage was segmented in the sagittal and coronal planes. The glenoid cartilage was segmented in the coronal plane. Group means for each region were calculated and compared between the groups.

Results: Massive tear group T2 values were significantly higher than the asymptomatic group values for the humeral head cartilage included in the sagittal (45 ± 7 versus 32 ± 4 ms, p < .001) and coronal (44 ± 6 versus 38 ± 1 ms, p = 0.01) plane images. Mean T2 was also significantly higher for massive than full-thickness tears (45 ± 7 versus 38 ± 5 ms, p = 0.02), massive than partial-thickness tears (45 ± 7 versus 34 ± 4 ms, p < 0.001), and massive tears than tendinosis (45 ± 7 versus 35 ± 4 ms, p = 0.001) in the sagittal-images humeral head region and significantly higher for massive tears than asymptomatic shoulders (44 ± 6 versus 38 ± 1 ms, p = 0.01) in the coronal-images humeral head region.

Conclusion: Humeral head cartilage T2 values were significantly positively correlated with rotator cuff pathology severity. Massive rotator cuff tear patients demonstrated significantly higher superior humeral head cartilage T2 mapping values relative to subjects with no/lesser degrees of rotator cuff pathology.

Abbreviations: GCor, glenoid, coronal plane; FS, fat suppressed; HH, humeral head; HHC, humeral head, coronal plane; HHSag, humeral head, sagittal plane; MRI, magnetic resonance imaging; PD, proton density; RC, rotator cuff; ROI, region of interest; SPACE, sampling perfection with application-optimized contrasts using different flip angle evolution; T2, transverse relaxation time; TSE, turbo spin echo.

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1. Introduction

Rotator cuff (RC) tears are common, and prevalence increases with age [1,2]. Although most RC tears remain asymptomatic [1] they can become symptomatic and can increase in size over time [3,4] and may become irreparable if untreated due to tendon atrophy and muscle fatty infiltration [5]. Late pathoanatomical changes characteristic of cuff tear arthropathy seen with massive RC tears include superior humeral head migration and erosion of the humeral head, glenoid, and acromion [6]. Less severe RC pathology such as tendinopathy and smaller tears have also been shown to be associated with degenerative changes of the glenohumeral cartilage [7–9]. It is debated whether RC pathology can act as prerequisite for glenohumeral osteoarthritis or vice versa [8]. However, it is clear that early osteoarthritic changes can lead to unfavorable clinical outcomes and increased re-tear rate following repair [9, 10]. This emphasizes the importance of detecting degenerative cartilage changes in patients with RC pathology at the earliest possible stage to achieve optimal outcomes and guide the timing of surgery.

The current standard imaging modality to detect cartilage degeneration is magnetic resonance imaging (MRI) [11]. Conventional MRI only provides information on late-stage OA-related morphological alterations of the cartilage [12–14]. However, before these macroscopic defects are visible, biochemical changes detectable by quantitative transverse relaxation time (T2) mapping occur in the cartilage matrix [15]. T2 mapping has made it possible to objectively evaluate these early biochemical cartilage changes before morphologic alterations appear [12,16,17].

Although T2 mapping has been studied extensively in knee cartilage [16,18–20], few studies exist on T2 mapping of the glenohumeral cartilage [12,14,15,21]. Recently, Lee et al. [13] have published a study on the T2 values of the glenohumeral cartilage in patients with rotator cuff disease. However, T2 values for the glenoid and humeral head were only assessed in a single plane, limiting T2 mapping coverage of the curved humeral head cartilage, and the spectrum of RC pathology studied did not include massive RC tears [13].

The purpose of this study was to evaluate the T2 mapping values for the entire mappable region of the glenohumeral cartilage in asymptomatic shoulders and in shoulders with supraspinatus tendon tendinosis, partial tears, full tears, and massive (multi-tendon) rotator cuff tears. The objective was to examine the relationship between glenohumeral cartilage T2 mapping values and rotator cuff pathology. We hypothesized that there would be differences in the T2 values between groups with different levels of RC pathology, with higher values for increasing severity of RC pathology.

2. Material and methods

2.1. Subjects

This study included 15 asymptomatic volunteers and 44 symptomatic clinical patient subjects (10 tendinosis, 13 partial-thickness tears, 8 full-thickness tears and 13 massive tears). This study was approved by the Institutional Review Board and written informed consent was obtained from all individual subjects in the asymptomatic subject group. The volunteer group included prospectively enrolled participants who were asymptomatic and had no prior shoulder injury or prior operative treatment in at least one shoulder. The uninjured participants were recruited between November 2012 and September 2015 by a research coordinator and informed consent was waived, with approval by the Institutional Review Board and HIPAA compliant access and handling of the patient data. The patient group included patients with rotator cuff tendinosis, partial-thickness tears, full-thickness tears, or massive tears imaged with T2 mapping MRI between May 2012 and September 2015. Inclusion criteria for the symptomatic cohort included patients who had failed nonoperative treatment, had undergone pre-operative T2 mapping MRI using the on-site 3 T scanner, and had subsequently arthroscopically confirmed rotator cuff pathology by the senior sports orthopedic surgeon showing either tendinosis, partial tearing of the supraspinatus with or without partial tearing of the infraspinatus, a full thickness tear defect of the supraspinatus tendon with or without accompanying partial tearing of the infraspinatus tendon with defect size of < 1 cm (with the proximal stump close to the bony insertion, Patte classification stage 1 [24]), or a massive rotator cuff tear, defined as full tearing of two to three rotator cuff tendons including the supraspinatus and either the infraspinatus and/or subscapularis, including both repairable and non-repairable tears). All groups except the massive tear group excluded subjects with prior surgical treatment to the injured shoulder. Exclusion criteria for all groups included insufficient image quality (due to motion or other artifact) or complete absence of visible cartilage on MR imaging. Summary characteristics of all subjects are listed in Table 1. Rotator cuff tendon T2 mapping data for all subjects except the massive tear subjects have been previously presented [23], but no cartilage data from these subjects have been published previously and all images were re-analyzed for this present study.

2.2. Image acquisition and processing

Unilateral shoulder images including morphological (either a volumetric fat suppressed (FS) PD-TSE sampling perfection with application-optimized contrasts using different flip angle evolution (SPACE) sequence acquired in the sagittal plane and subsequently reformatted for evaluation in the sagittal and coronal planes, or two-dimensional sagittal and coronal PD TSE FS sequences), and sagittal and coronal multi-echo spin-echo T2 mapping images (repetition time: 2000 ms, echo times: 10.7, 21.4, 32.1, 42.8, 53.5, 64.2, and 74.9 ms, field of view: 140 mm, matrix: 256 × 256, voxel size: 0.55 × 0.55 × 2.00 mm, slice spacing: 3.00 mm (2.00 mm slice thickness with 1.00 mm gap), number

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Table 1

| Group          | N | Age (mean ± standard deviation) [years] | Sex   | Prior operation                     |
|----------------|---|----------------------------------------|-------|------------------------------------|
| Asymptomatic   | 15 | 36 ± 13                                | 7 F, 8 M |                                    |
| Tendinosis     | 10 | 45 ± 10                                | 5 F, 5 M | N/A                                |
| Partial tear   | 13 | 47 ± 8                                 | 5 F, 5 M |                                    |
| Full tear      | 8  | 58 ± 8                                 | 5 F, 3 M |                                    |
| Massive tear   | 13 | 60 ± 8                                 | 6 F, 7 M | 2 arthroscopic cuff repair,         |

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of slices: 20–22 (coronal), 18–20 (sagittal), examination time: 6:30 for each plane) were obtained for all subjects. The sagittal and coronal planes were used to provide a perpendicular imaging plane to the glenoid cartilage (coronal plane) and orthogonal planes to provide good visualization of the curved humeral head cartilage (coronal plane for visualization of the inferior to superior central portion of the cartilage and the sagittal plane for visualization of the anterior and posterior portions of the superior region of the cartilage). These two planes have been used in prior work focused on T2 mapping of the glenohumeral cartilage [15].

Images were acquired using a Siemens Magnetom Verio 3 T scanner (Siemens Medical Solutions, Erlangen, Germany) with a gradient strength of 40 m T/m, using a four-channel shoulder array receive coil (Invivo, Gainesville, FL, USA). Subjects were positioned supine with the imaged arm at their side. T2 values were calculated from a decay curve including all mapping echoes using a pixel-wise, mono-exponential, non-negative least square fit analysis algorithm (Siemens MapIt; Siemens Medical Solutions, Erlangen, Germany). The resulting T2 mapping images were exported.

For each subject manual segmentation of the glenoid and humeral cartilage was conducted on each slice of the second echo of the T2 mapping sequence (TE = 21.4 ms) by two raters, using a stylus and touchscreen (WACOM Cintiq; Wacom Technology Corporation, Portland, OR, USA) in Mimics software (Materialize, Plymouth, MI, USA). A single rater performed two rounds for each subject to allow evaluation of intra-rater reliability. The two rounds were separated by at least two weeks to reduce potential bias. Raters included three orthopedic research assistants (one premedical student and two medical students) and one orthopedic surgeon with 6 years of experience. All raters were trained with feedback from a senior musculoskeletal radiologist with 30 years of experience and a research engineer with 4 years of experience. The humeral head cartilage was segmented in both the sagittal and coronal planes, while the glenoid cartilage was segmented only in the coronal plane owing to its orientation parallel to the sagittal plane. The raters were instructed to include cartilage that could be clearly visualized on the second echo of the T2 mapping sequence, excluding regions where the cartilage curved into the plane of the image and the articular surface was no longer distinct. The resulting number of slices segmented was generally between 5 and 9 slices. The sagittal humeral head (HHSag) segmentation region included the superior humeral head cartilage including anterior and posterior portions. The coronal humeral head (HHCor) segmentation included the entire glenoid cartilage surface. The fat-suppressed morphological images were used as a reference to assist in excluding synovial fluid and chemical shift artifact. Fig. 1 shows an example of the PD TSE FS reference image, the second echo T2 mapping image with overlaid segmentation, and the T2 map image.

The humeral head and glenoid masks were exported from Mimics as binary images and imported into a custom MATLAB program (MATLAB Release 2013a, The MathWorks, Natick, MS, USA) along with the corresponding T2 maps exported previously from the MapIt software. The binary cartilage segmentations were automatically overlaid onto the T2 map images to define the appropriate region of interest (ROI) pixels on the corresponding T2 map images. Summary T2 parameters (mean, median, minimum, maximum, and number of pixels) for each masked region of interest were then calculated. The subject median T2 mapping values within each region were calculated, and the group means and standard deviations of these values were calculated and used for between-group comparisons.

All statistical analysis was performed using the statistical package R (R Development Core Team, Vienna, Austria) [25]. The rater reliability, as generalizable to a single future rater, was evaluated over a subgroup of 14 subjects between separate single rounds for one rater (intra-rater) and between two different raters (inter-rater) using the intra-class correlation coefficient (ICC) for a two-way random effects model of absolute agreement. Between-group comparisons were performed by a biostatistician to examine cartilage T2 map value differences between the five subject groups. The subject group mean T2 values were compared for each cartilage ROI in parallel using parametric analysis of variance (ANOVA) with Tukey pairwise post-hoc comparisons. P-values less than .05 were considered statistically significant. A Spearman’s rank correlation test was used to look for monotonic correlations between age and T2 values, and between age and pathology grade, where the five subject groups were represented by numeric values 1–5 in order of increasing pathology severity.

### 3. Results

The intra-class correlation coefficient (ICC) for absolute agreement for each region were 0.82 (GCor), 0.90 (HHCor), and 0.86 (HHSag) for intra-rater agreement and 0.84 (GCor), 0.83 (HHCor), and 0.92 (HHSag) for inter-rater agreement. These values all fall within the “excellent” reliability category as described by Fleiss [26] (0.75–1.00 = excellent reliability, 0.40–0.75 = fair to good reliability, and 0–0.40 = poor reliability). Table 2 summarizes the agreement ICCs, ICC confidence intervals, bias, and limits of agreement.

The mean cartilage T2 values for each subject group are shown in Table 3. Mean T2 values for all ROIs were lowest in the shoulders of asymptomatic volunteers (HHSag: 32 ± 4 ms; HHCor: 38 ± 2 ms; GCor: 36 ± 4 ms) and highest for the shoulders of patients with massive tears (HHSag: 45 ± 8 ms; HHCor: 44 ± 6 ms; GCor: 41 ± 4 ms). For the HHSag region the massive tear group T2 mapping values were significantly greater than for the full-thickness tear group (45 ± 7 versus 38 ± 5 ms, p = .02), the partial tear group (45 ± 7 versus 34 ± 4 ms, p < .001), the tendinosis group (45 ± 7 versus 35 ± 4 ms, p < .001) and asymptomatic group (45 ± 7 versus 32 ± 4 ms, p < .001) (Fig. 2). For the HHCor region the mean T2 values only differed significantly between the massive and

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Fig. 1. Images from one example subject from the massive tear group (59 year-old woman) showing (A) PD TSE FS COR reference image for one slice, (B) the corresponding T2 mapping second echo image with overlaid segmentation masks in green (humeral cartilage) and yellow (glenoid cartilage) overlaid, and (C) the T2 map image with color-scale.
The most important finding of this study was that the superior humeral head cartilage, as evaluated on the sagittal T2 mapping images, showed significant differences in T2 values between the massive tear rotator cuff pathology group and the groups with no rotator cuff pathology and less severe rotator cuff pathology. Furthermore, the cartilage T2 mapping values for all mapped regions of the glenohumeral cartilage tended to be higher with increasing rotator cuff pathology compared to the values of asymptomatic volunteers, with significant positive correlation between median T2 values and rotator cuff pathology severity for the HHSag and HHCor regions.

4. Discussion

The most important finding of this study was that the superior humeral head cartilage, as evaluated on the sagittal T2 mapping images, showed significant differences in T2 values between the massive tear rotator cuff pathology group and the groups with no rotator cuff pathology and less severe rotator cuff pathology. Furthermore, the cartilage T2 mapping values for all mapped regions of the glenohumeral cartilage tended to be higher with increasing rotator cuff pathology compared to the values of asymptomatic volunteers, with significant positive correlation between median T2 values and rotator cuff pathology severity for the HHSag and HHCor regions.

Rotator cuff pathology is a common condition and prevalence increases with age [1,2] with over one in six asymptomatic individuals aged 60–69 years and approximately four in six symptomatic patients in the same age group having rotator cuff abnormalities [1]. Glenohumeral osteoarthritis is often seen in conjunction with rotator cuff pathology [7–9], and can produce similar symptoms, making correct diagnosis of the pain generator challenging in many patients. Furthermore, surgical treatment strategies change once the shoulder becomes arthritic. Although it is debated whether osteoarthritis is a prerequisite or result of rotator cuff pathology, it is well understood that osteoarthritic changes result in unfavorable outcomes following rotator cuff repair [8–10].

When glenohumeral cartilage changes are seen macroscopically (e.g. during surgery), the cartilage damage process is well underway [12]. The same applies to current imaging modalities that are used to directly or indirectly evaluate the cartilage, such as conventional MRI or radiography, as these show late macroscopic morphologic changes of the cartilage only. Therefore, it is desirable to detect early cartilage damage through noninvasive means such as quantitative MRI and to consider cartilage health when determining the appropriate timing for rotator cuff repair.
cuff repair and other glenohumeral joint treatments. T2 mapping MRI has been shown to be sensitive to early changes in articular cartilage water and collagen content and tissue anisotropy [17], which are known to precede morphologic changes [12, 16], and thus may enable detection of early cartilage damage in the glenohumeral joint in rotator cuff patients.

Kang et al. [12] were the first to report on T2 values of the glenohumeral joint cartilage in asymptomatic individuals, using the oblique coronal plane, and demonstrated good intra-observer agreement (ICC 0.736). They reported a mean humeral T2 value 50.5 ± 12 ms and mean glenoid T2 value 49.0 ± 9.9 ms. Subsequently, Lockard et al. reported on glenohumeral T2 values in 21 asymptomatic volunteers and introduced the sagittal plane for increased mapping coverage of the anterior and posterior regions of the superior humeral head cartilage, which was unreported previously [15]. They reported a mean glenoid T2 cartilage value of 38 ± 2 ms, a mean humeral head T2 value of 41 ± 3 ms (coronal) and 34 ± 2 ms (sagittal). Fair-to-good and excellent intra- and interrater reliability values were reported, similar to Kang et al. [12].

In patients T2 mapping has been used to look at glenohumeral osteoarthritis and focal cartilage damage. Lee et al. [14] compared the median T2 values of patients with glenohumeral osteoarthritis to patients with normal macroscopic cartilage and demonstrated significantly higher total (glenoid and humeral head combined) T2 values for patients with osteoarthritis (median 37.52 ms; range 36.84–39.11 ms) compared to patients without (median 36.00 ms; range 33.89–37.31 ms). Wuehmann et al. [21] examined the ability of T2 mapping MRI to detect focal changes in glenohumeral cartilage, with validation performed by arthroscopy in 18 patients (5 with cartilage lesions). They found that T2 mapping mean values were significantly higher in the locations of the Outerbridge grades 1–3 lesions (44.7 ± 3.7 ms) than in regions of cartilage that appeared healthy on arthroscopic examination (23.0 ± 3 ms).
Research applying T2 mapping to evaluation of cartilage health in shoulders with rotator cuff pathology has been limited. However, Lee et al. [13] recently conducted a study performing T2 mapping of the glenohumeral cartilage in 62 patients with varying degrees of rotator cuff pathology (grade 1: normal to tendinosis; grade 2: partial-thickness tear; grade 3: full-thickness tear) and fatty degeneration according to the Goutallier classification (grades 0 through 4). Similar to this present study they found no significant differences in mean T2 values between the different degrees of rotator cuff tears within the normal to full-thickness, non-massive-tear groups. Unlike in the present work, they grouped normal and tendinosis patients and did not separate out massive tear subjects. Lee et al. did find that fatty atrophy grade 3 correlated with higher T2 values of the glenoid cartilage. They reported low interobserver reproducibility (ICC agreement, glenoid: 0.501; humeral head: 0.721) between the two raters and used only three coronal slices for each subject in their investigation [13], limiting evaluation of the superior humeral head cartilage to a thin (9.9 mm wide) central coronal section.

This present work provides a more comprehensive analysis of the relationship between T2 mapping values and rotator cuff pathology grade by including an asymptomatic, uninjured control group and incorporating a massive tear subject group. In contrast to some prior studies, in this work we used the median T2 values for each subject and region as the summary statistic of interest to decrease the influence of outlier voxels that include non-cartilage tissue or noise signal and have an outsized impact on the mean T2 value within a cartilage region. In addition, this present study included greater imaging coverage of the glenohumeral cartilage than in prior studies. We included the sagittal plane of the humeral head and utilized all possible slices of the respective planes to maximize coverage and evaluation of the cartilage. By maximizing cartilage coverage, we were able to observe spatial patterns in T2 mapping differences between the rotator cuff pathology severity groups. We found that the superior humeral head cartilage (HHSag region) showed the greatest differences between the massive rotator cuff tear group and the groups with no or lesser rotator cuff pathology, which align with the findings of previous histological analyses of cadaver and total shoulder arthroplasty patient glenohumeral articular surfaces, and previous quantitative MRI pilot study findings. Cadaveric research on donors with rotator cuff pathology has shown that gross macroscopic osteoarthritic changes occur in specific patterns, with the anterosuperior [7] and anteroinferior [7,27] quadrants of the glenoid and the anteroinferior [7,27] and posteroinferior [7] quadrants of the humerus being predominantly affected. A recent histologic study in living patients has confirmed these findings, showing osteoarthritic changes specifically in the superior part of the humeral head for cuff tear arthropathy patients undergoing shoulder arthroplasty [28]. Okada et al. [29] found a similar spatial pattern of cartilage alteration on coronal T1 rho mapping of the humeral head cartilage in a pilot study of 10 healthy volunteers and 10 patients with small- to medium-sized rotator cuff tears, with higher T1 rho values in the rotator cuff patients when compared to the uninjured subjects in the middle-to-superior portion of the humeral head cartilage [29]. In our work this pattern may have been most evident in the massive tear group due to T2 mapping being sensitive to more advanced early cartilage damage compared to T1 rho [30].

Our study does not come without limitations. First, our study was performed retrospectively and therefore includes a risk of selection bias. There was a trend of increasing age with increasing severity of pathology, which introduces the effect of age-related cartilage T2 mapping value changes in addition to those due only to the pathology. The strength of correlation was found to be similar for the pathology grade and median T2 correlation and the pathology grade and median T2 correlation. Despite attempting to adjust for age via analysis of covariance (ANCOVA), the multicollinearity was unresolvable, and we were not able to disambiguate between age and pathology as independent predictors of T2 values. Another selection bias was that for the massive tear group four of the 13 subjects were imaged postoperatively. Operative treatment may have a separate impact on cartilage health, although in this study the preoperative and postoperative massive tear subgroups had similar T2 values (40 ± 4 ms versus 39 ± 5 ms, 44 ± 6 ms versus 45 ± 6 ms, and 45 ± 7 ms versus 47 ± 8 ms for the preoperatively images versus postoperatively imaged group coronal glenoid, coronal humeral head, and sagittal humeral head cartilage, respectively). The finding of higher mean cartilage T2 in the tendinosis subject group relative to the partial tear and/or full tear group mean T2 value was unexpected and may be due in part to the study limitations of small group size, potential selection bias, and variable group age ranges.

The MRI T2 mapping measurements were limited by relatively large pixel size (0.55 × 0.55 mm) relative to the cartilage thickness, and partial volume averaging both at the articular cartilage superficial and deep surfaces and where the cartilage curved into the plane of the images. Because T2 mapping requires relatively thick slices (2-3 mm generally), curved articular surfaces such as those of the humeral head are more challenging to map, particularly near the edges of the region. Lastly, due to the thick-slice images and lack of precise shoulder landmarks visible on the T2 mapping images evaluation of additional, smaller subregions of the humeral head and glenoid cartilage was not performed as part of this work. Smaller subregions have been used previously in the study of focal glenoid cartilage defects and would be beneficial for detecting more localized changes [21]. Use of high-resolution sequences along with the T2 mapping sequence could address this challenge in future studies.

5. Conclusions

In summary, we found that quantitative T2 mapping of the glenohumeral cartilage showed a tendency towards higher T2 values with increasing severity of rotator cuff pathology, and that the superior humeral head cartilage captured by the sagittal plane images showed the greatest number of significant differences between massive tear subjects and those with no or lesser levels of rotator cuff pathology. These findings suggest that the superior humeral head cartilage may be most susceptible to damage in massive rotator cuff tear patients and that T2 mapping MRI in the sagittal plan allows quantification of these cartilage changes and may aid in early identification of these cartilage changes.

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CRediT authorship contribution statement

Carly A. Lockard: Conceptualization, Data curation, Investigation, Methodology, Formal analysis, Visualization, Writing - original draft, Writing - review & editing. Philip-C. Notte: Investigation, Formal analysis, Visualization, Writing - original draft, Writing - review & editing. Karissa M.B. Gawronski: Investigation, Visualization, Writing - original draft, Writing - review & editing. Bryant P. Erick: Investigation, Visualization, Writing - original draft, Writing - review & editing. Brandon T. Goldenberg: Investigation, Visualization, Writing - original draft, Writing - review & editing. Marilee P. Horan: Data curation, Investigation, Writing - review & editing. Grant J. Dorman: Formal analysis, Visualization, Writing - review & editing. Charles P. Ho: Conceptualization, Investigation, Methodology, Writing - original draft, Writing - review & editing. Peter J. Millett: Conceptualization, Investigation, Methodology, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The authors declare no conflict of interest.
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