Optimization of Image Registration and Application to Human Disc Mechanics with Nucleotomy

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Abstract—**Introduction: Advanced Normalization Tools (ANTs) is an image registration program that has been validated for analysis of several tissues, but not previously applied to the disc. The objectives of this study were to optimize ANTs for disc image registration and to validate ANTs strain measurements by comparison with Vic2D, a commercially available software previously applied to quantify disc strain, before and after nucleotomy. Methods: Human lumbar motion segments (n=5) underwent 1000 N compression before and after nucleotomy and MR images were acquired in a reference and deformed state. Image overlap statistics were used to select mapping parameters, and strain analysis was used to select the optimal number of splines. Once the optimal registration method was selected (elastic mapping, 0.01 outlier, 6x6 splines), axial and radial strains were measured in the AAF, PAF, and IVD. Results: Excellent overlap statistics were achieved. No significant differences were found for strains calculated with ANTs and Vic2D ($p \geq 0.35$). With nucleotomy, the axial compressive strain increased in the PAF ($p=0.04$) and there was a trend towards decrease in radial strain ($p=0.07$). Discussion: ANTs is an accurate and powerful tool to calculate disc strains from MR images.**

I. Introduction

Disc degeneration can be modeled *in vitro* by nucleotomy to study altered disc mechanics. Recently, we developed a noninvasive technique to quantify internal disc strains from 2D magnetic resonance (MR) images utilizing the texture correlation software Vic2D [1] and applied it to evaluate disc mechanics before and after nucleotomy [2]. Strain could only be calculated in small rectangular areas of interest with Vic2D, missing regions at the bone–disc interface. Advanced Normalization Tools (ANTs), an image registration software, creates a continuous map of the transformation between images and, with manual segmentation tools, can obtain strain measurements across any user-defined region, and the B-spline regularization model has been used to quantify myocardial strain in the heart [3]. The objectives of this study were to optimize the ANTs B-spline model for disc image registration and validate ANTs strain measurements before and after nucleotomy through comparison with Vic2D.

II. Methods and Materials

A. Optimization of Image Registration Parameters

Intact fresh-frozen human lumbar motion segments (n=5, grade 1-3) underwent compression inside an MR scanner [1]. Mid-sagittal images were acquired before (original) and after the application of 1000N load (deformed). Key anatomic features that could be visualized in both images were labeled using manual segmentation software ITK-SNAP (Fig 1A) [4].

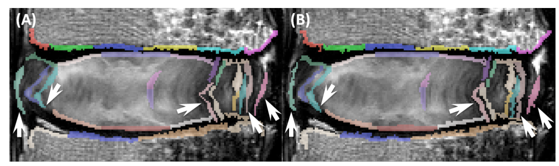

Fig. 1: Representative (A) intact and (B) warped labeled images. Arrows indicate differences between original and warped

Sixteen registrations were performed on the labeled images with different mappings, outliers, and numbers of splines. Mapping controls the type of deformation in the transformation and the outlier accounts for noise. Registration parameters were first optimized with overlap statistics [5] between original and reconstructed (warped) labels (Fig 1B). Target overlap is the ratio of the area contained in both the original and warped labels over the area of the original label. Hausdorff measures the degree of mismatch between two labels, and is calculated as the maximal distance of all pixels in the original label to the nearest point in the warped label. Average Hausdorff is the average of all pixel distances between both labels. Labels were grouped into superior/inferior vertebral body (SVB/IVB), anterior/posterior annulus fibrosus (AAF/PAF), or nucleus pulposus (NP), and each overlap statistic (avg. ± st. dev.) was calculated across these regions. The optimal mapping and outlier were determined by ranking the registrations according to the overlap statistic measures for each image pair.

The optimal spline number (from 2x2 to 14x14) was then determined by repeating the registration with the mapping and outlier parameters determined above. Radial and axial annulus strains from the anterior and posterior (avg. ± st.dev.) were plotted against the number of splines to determine the optimal number (Fig 2).

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B. Nucleotomy Strain Analysis and Validation

Each disc (n=5) underwent mechanical loading in the MR after nucleotomy, as previously published using Vic2D texture correlation [2]. Original and deformed images of intact discs and discs after nucleotomy were segmented into regions: AAF and PAF in ITK-SNAP. The optimal registration (Section III) was performed with ANTs. Axial and radial strains (avg. ± st. dev.) were calculated in each region and strain maps were generated using the ANTs. Paired two-tail t-tests were performed comparing strains in the AAF and PAF between intact vs nucleotomy data and ANTs vs Vic2D [2] ($p \leq 0.05$).

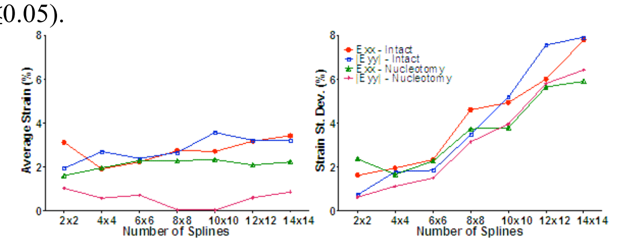

Fig. 2: Representative plot on the effect of B-splines on AAF and PAF (A) Avg (B) St. dev. for axial and radial strain

III. Results

A. Optimization of Image Registration Parameters

The optimal registration was determined to be B-spline regularization with elastic mapping, outlier of 0.01, and 6x6 splines. The elastic mapping was optimal in four of the five image pairs and an outlier of 0.01 was optimal for all cases. This registration had 68.90% target overlap, Hausdorff of 2.19 pixels, and Average Hausdorff of 0.36 pixels.

B. Nucleotomy Strain Analysis and Validation

Strain standard deviation increased with the number of splines, while the average strain remained relatively constant between registrations (Fig 2). The 6x6 splines were selected as the average was stable with a lower standard deviation.

The axial compressive strain increased in the PAF ($p=0.04$) and radial strain tended to decrease ($p=0.07$) for intact compared to after nucleotomy (Fig 3). No significant difference in strain was observed for registrations using ANTs and Vic2D for any groups or regions ($p \geq 0.35$).

IV. Discussion

This study is the first time ANTs image registration has been used to measure intervertebral disc mechanics. In the B-spline model, a higher number of splines resulted in less smoothing within the strain map. Increasing the number of splines caused the strain standard deviation to rise while the strain averages stayed relatively constant. When the optimal mapping and outlier was used, increasing numbers of splines caused the target overlap to vary by less than 2% and the Hausdorff by less than 0.1 pixels, confirming that feature detection was not compromised by choosing 6x6 splines.

With 234 µm/pixel image resolution, Hausdorff indicates a maximum shift of 500 µm between original and deformed labels (approximately the width of one lamella), while the Average Hausdorff reports an average shift of 80 µm. The original and warped labels overlapped by approximately 70%; slight variances can be seen from original to warped (arrows Fig 1). Ideally overlap would be 100%, but this was not achieved due to human error in visualizing and marking anatomic features. The MR images had poor contrast between certain structures and image artifacts. Key anatomic features became more or less prominent in deformed images as individual substructures such as AF lamellae moved in and out of plane. Since these issues compromised the ability to create accurate labels, we conclude that ANTs' accuracy is greater than indicated in the overlap statistics.

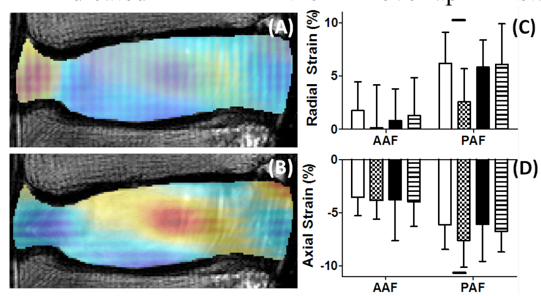

Fig. 3: Representative (A) radial and (B) axial strain maps generated in ANTs. (C) Radial strains and (D) Axial strains measured in the AAF, PAF, and IVD in ANTs (intact white, nucleotomy checkered) and Vic2D (intact black, nucleotomy striped), == $p \leq 0.05$ & — $p \leq 0.10$.

This study established optimal parameters for ANTs image registration of the disc and validated strain measurements before and after nucleotomy through comparison with strains from Vic2D image registration [2]. With nucleotomy, axial PAF strain increases when quantified with both Vic2D [2] ($p=0.06$) and ANTs. Strain values were comparable between both techniques, with Vic2D yielding a 30% increase and ANTs a 24% increase in axial strain as a result of nucleotomy in the PAF. The effect radial strain in the PAF post nucleotomy was also similar to Vic2D, which found a decrease of 50% ($p=0.01$) while ANTS showed a decrease of 58%.

There were no significant differences between ANTs and Vic2D, however, the observed slight variance between them are likely due to ANTs' ability to measure strain across the entire region of interest, potentially including areas that underwent greater deformation.

Acknowledgment

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