Toward quantitative biomarkers of cervical structural health: development of MRI tools for in-vivo mechanical property measurement.

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PURPOSE

In the condition known as Cervical Insufficiency (CI), the cervix dilates and shortens prematurely, resulting in delivery of the fetus as early as the second trimester. The mechanical properties of cervical tissue and cervical geometry are crucial factors in the ability of the cervix to withstand mechanical loading from the fetus during the course of pregnancy. It is known that cervical tissue undergoes a remodeling process during pregnancy that changes its biochemical composition. Cervical tissue comprises primarily water (approx. 80% w/v), extracellular matrix (ECM) components such as cross-linked collagen types I and III, proteoglycans, and elastin [1-2].

Previous work by our group has quantified the ex-vivo mechanical stress response and hydraulic permeability of cervical tissue specimens from pregnant (PG) and non-pregnant (NPG) women [3-4]. We found that mechanical properties are different between PG and NPG specimens, and can vary greatly within the PG and NPG sample groups, underscoring the need for patient-specific assessment. At present, there is no widely accepted quantitative measure of cervical tissue strength. Due to the role of fluid transport in dictating the mechanical response of hydrated tissues, diffusion based MRI modalities are poised to provide valuable information to predict a tissue's mechanical response to load by characterizing that tissue's nonlinear relationship between random molecular diffusion of fluid and bulk interstitial fluid movement.

The purpose of this study was to explore the coupled relationship between the diffusive properties of a hydrated material (via ADC) as measured by MRI and its corresponding hydraulic permeability measured in-vitro. These results for polyacrylamide hydrogels are a foundation for the characterization of similar relationships in human cervical tissue which can potentially be used as quantitative clinical biomarkers for cervical mechanical properties and preterm birth risk.

METHODS

A phantom with polyacrylamide hydrogels (1:19 bis:acrylamide ratio) ranging from 3 to 30% (v/v) polyacrylamide/H_2O was created. A full body Philips 3T Achieva scanner with 8-channel head coil was used to scan the phantom at room temperature. Diffusion weighted images were acquired with a single-shot spin echo (SE-EPI) sequence (TR/TE=2000/57 ms, matrix size=112x89, SENSE factor=2, slice thickness=2mm, gap=1mm, 7 slices, total scan time=2m30s) using multiple b-factors (0, 10, 20, 40, 80, 120, 160, 200, 240, 300, 500, 800, 900, 1000, 1200, 1500 s/mm^2) and diffusion sensitizing gradients in 3 orthogonal directions. A mono-exponential fit was performed to generate ADC maps from the data.

Hydraulic permeability measurements of separate polyacrylamide hydrogel phantoms with the same concentrations (3-30% v/v) were performed using a custom permeation experiment developed in our lab [4] and originally used to measure the permeability of human cervical tissue. The experiment applies a fluid pressure gradient across a specimen and measures the resulting flow rate, giving the permeability.

RESULTS

All image analysis on ADC maps was performed using Osirix [5], an open source image viewer. ROIs were created inside each phantom on all three slices centered within the phantoms. Mean ADC and standard deviation were recorded in each ROI for each specimen, and the results were fitted to a linear curve using least squares regression (R^2=0.995). Over three slices, ROI average ADC values all had a standard deviation within 2% of the mean. ADC was observed to decrease linearly with increasing polyacrylamide concentration, consistent with expectation. Permeability was found to *decrease* exponentially with linearly *increasing* polyacrylamide concentration (R^2=0.986). This trend was stronger after corrections were made for gel concentration using the dry weight of each specimen.

DISCUSSION

Research on the relationship between hydraulic permeability and MRI ADC is limited. In this study, a strong correlation between ADC and permeability has been characterized in polyacrylamide hydrogels.

CONCLUSION

Future ADC and permeability tests planned for ex-vivo cervical specimens in the near future will provide data on any similar relationship that may exist for cervical tissue. Cervical ADC might be able to quantify permeability differences linked to microstructural organization and tissue strength. Additionally, diffusion tensor data will be paired with direction-dependent permeability tests on grown collagen scaffolds to learn about the impact of microstructure directionality on this technique.

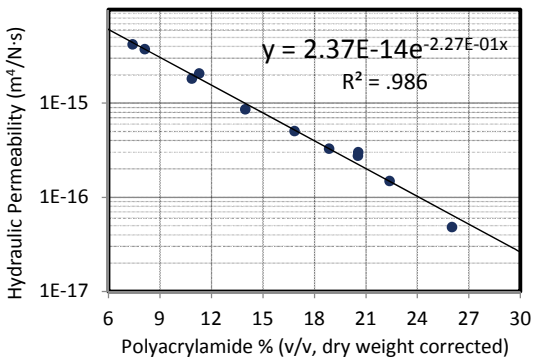

Figure 1: Permeability vs. Polyacrylamide % Concentration. 3% uncertainty in semilog slope (95% conf.).

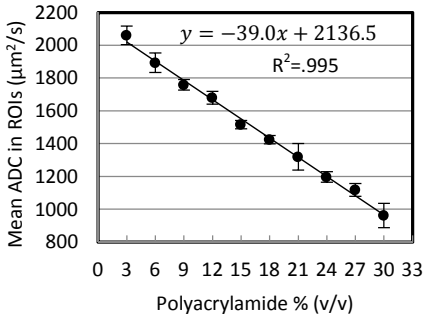

Figure 2: Mean ADC in ROIs vs. Polyacrylamide % Concentration. 2% uncertainty in slope (95% conf.). Error bars represent standard deviation of voxel data.

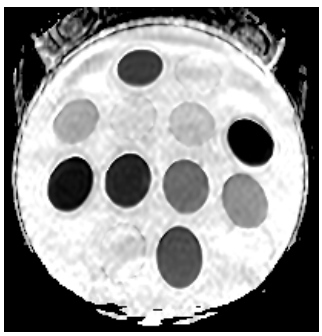

Figure 3: Example ADC Map with polyacrylamide phantoms inside gelatin surroundings. The entire phantom is 6" in diameter.

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