

This is a proposal to develop new approaches to image registration for the purpose of detecting and tracking low contrast soft tissue lesions from multiple ultrasound scans. While the methods to be developed will have wide applicability to many other types of imaging modalities and applications our methods will be tested and validated on ultrasound images of breast and musculo-skeletal tissues. Accurate registration of multiple medical image scans is essential for detection of functional and anatomical anomalies and assessment of the evolution of such anomalies over time. For example in whole breast imaging, registration of 3D breast ultrasound image volumes is essential to detecting small breast lesions; discrimination of malignant from benign lesions; detection of secondary masses; and quantifying response to treatment. Advances in image registration of breast images will have substantial societal impact as typical community practitioners currently miss asymptomatic breast lesions in up to 45% of women with dense breasts. Accurate registration is also important for tracking the evolution of muscle tears and sprains, tendon and muscle inflammation, post-surgical recovery and other areas in sports medicine and physical rehabilitation.

Investigation of ultrasound image registration is relatively new and not widespread. Only recently, with single voxel mutual information techniques, has such registration appeared to be very promising. However, these registration methods have proven overly sensitive to spurious image components and artifacts due to speckle, shear/compressive tissue deformation, and shadowing which are ubiquitous to modalities such as ultrasound imaging. As ultrasound is a cheap and widely available diagnostic imaging modality, improving image registration can have wideranging medical impact. The significantly improved registration methods outlined in this proposal may be a critical key to making routine serial ultrasound studies of soft tissues practical and informative.

This 3 year grant proposal describes a new and powerful approach to image registration which uses stable higher order image features in addition to single pixel or single voxel gray scale levels. In so doing we can capture complex spatial information that is ignored in the current state of the art single pixel mutual information and correlation-based registration techniques. Further, this spatial information can permit more accurate and robust image and image volume registration which overcomes the limiting sensitivities of previously proposed registration techniques to spurious artifacts. Here we offer convincing evidence that inclusion of such information may be the key to extending the single-pixel mutual-information registration techniques to a new level of effectiveness for diagnostic ultrasound.

We take a systematic approach to developing mathematical image registration algorithms which combines the latest advances in inductive learning, information theory, pattern matching, graph theory, and statistical classification. We propose to apply a matching method which is provably optimal, in terms of minimizing a bound on misclassification probability. We propose to perform feature selection using state-of-the-art inductive learning methods including randomized feature classification trees and randomized independent component analysis (ICA). We propose to evaluate the goodness of match between a pair of images from the coincidences of their spatially localized features. We propose to develop novel and fast methods for registration based on minimal spanning graph algorithms and a new registration function as a feature matching criterion: the  $\alpha$ -mutual information. Finally, we propose extensive validation of our new registration method on a database of previously acquired patient scans of breast and other soft tissues. The PI and co-PI partnership between a leader in image processing and a leader in diagnostic ultrasound makes a leap forward possible in image registration for ultrasound imaging. This interdisciplinary project will also contribute to graduate education by cross-disciplinary training of a graduate student in the engineering and biomedical sciences.