Enhanced ultrasound for advanced diagnostics, ultrasound tomography for volume limb imaging and prosthetic fitting

Brian Anthony
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Brian W. Anthony*
Massachusetts Institute of Technology, 77 Massachusetts Ave, Cambridge MA, 02139

ABSTRACT

Ultrasound imaging methods hold the potential to deliver low-cost, high-resolution, operator-independent and non-ionizing imaging systems – such systems couple appropriate algorithms with imaging devices and techniques. The increasing demands on general practitioners motivate us to develop more usable and productive diagnostic imaging equipment. Ultrasound, specifically freehand ultrasound, is a low cost and safe medical imaging technique. It doesn't expose a patient to ionizing radiation. Its safety and versatility make it very well suited for the increasing demands on general practitioners, or for providing improved medical care in rural regions or the developing world. However it typically suffers from sonographer variability; we will discuss techniques to address user variability.

We also discuss our work to combine cylindrical scanning systems with state of the art inversion algorithms to deliver ultrasound systems for imaging and quantifying limbs in 3-D in vivo. Such systems have the potential to track the progression of limb health at a low cost and without radiation exposure, as well as, improve prosthetic socket fitting. Current methods of prosthetic socket fabrication remain subjective and ineffective at creating an interface to the human body that is both comfortable and functional. Though there has been recent success using methods like magnetic resonance imaging and biomechanical modeling, a low-cost, streamlined, and quantitative process for prosthetic cup design and fabrication has not been fully demonstrated. Medical ultrasonography may inform the design process of prosthetic sockets in a more objective manner. This keynote talk presents the results of progress in this area.

Keywords: Clinical ultrasound, Force control, 3-D ultrasound, Tomography

1. INTRODUCTION

The increasing demands on general practitioners motivate us to develop more usable and productive diagnostic imaging equipment. Ultrasound, specifically freehand ultrasound, is a low cost and safe medical imaging technique. It doesn't expose a patient to ionizing radiation. Its safety and versatility make it very well suited for the increasing demands on general practitioners, or for providing improved medical care in rural regions or the developing world. Ultrasound is used to image soft tissues of the body. Because of its benign nature it is used extensively in medicine. Recent computational advances have reduced the size of ultrasound imaging equipment to the point where handheld devices are available from a variety of major industrial vendors. Operator dependence is a significant factor limiting deployment of diagnostic ultrasound throughout all of medicine and into the broader community.

As shown in Figure 1 the process of acquiring clear, diagnostically-useful ultrasound images requires a trained clinician to actively interpret the imagery during the image acquisition process. The clinician holds an ultrasound probe in contact with the patient. The clinician slides the probe along the patient’s skin and presses the probe into the body, continuously sliding, rotating, and exerting force in order to create a good diagnostic image. This keynote talk highlights our research which occurs in the areas shown in blue in Figure 1. We work to enhance the imaging workflow by measuring and controlling the acquisition state and by analyzing the combination of state information and US images to extract additional quantitative information from the US image data. In this way we can provide additional guidance to the clinician, and help control the imaging hardware, all with a goal of improving image interpretation and quantitative analysis.

Our hypothesis is that, ultrasound imagery, when acquired under a controlled or measured state - such as known or maintained contact pressure, or known or maintained orientation and position with respect to the patient - provides image context data and imaging-process context data that can be used to enable new, and to improve existing, clinical applications of ultrasound. We add force measurement sensors, a handheld motion stage platform, and the ability to control the force applied to the patient through an ultrasound probe; this technology can be used to enhance clinical application of

* banthony@mit.edu; phone 1 617 324 7437; devicerealization.mit.edu
elastography, measure blood-pressure, or to automatically compensate for patient or clinician motion. We add cameras, accelerometers, and gyroscopes to hand-held probes and fixed-frame imaging systems to estimate the orientation and pose of the probe with respect to the patient body; this technology enables placement of the ultrasound transducer in the same patient-body location by different operators on serial examinations and large volume acquisitions - enabling series examination of muscle health, post-acquisition re-slicing and reformatting of volume data, and addresses clinical imaging needs in limb health.

![Figure 1. Ultrasound System Flow](image)

In this keynote talk we review several technology innovations that measure or control aspects of the ultrasound system and briefly highlight the clinical applications that these technologies enhance and enable.

2. FORCE VARIATION

2.1 Sonographer Variation

Variations in ultrasound probe contact force from one operator to another or from one moment to another lead to variations in ultrasound images which make the images difficult to directly and quantitatively compare with each other. The contact force required to obtain an ultrasound image deforms the underlying soft tissue. Conventionally, the probe-patient contact force is controlled qualitatively by the human operator. We have developed a force-measurement platform, Figure 2, which can simultaneously image and measure precise, operator-applied, force. We have demonstrated that during an ultrasound exam contact forces exerted by the operator can vary, up to 50% over 30 seconds\(^1\), resulting in images that are acquired at different levels of tissue deformation. We have used the force measurement platform to explore the impact of preload on elastic property estimates of Young’s modulus in tissue and to characterize the average preload applied during abdominal sonography – it varies between 4.4 and 10 Newtons\(^2\). Preliminary analysis reveals trends in applied force versus years of experience and BMI of the patient\(^2\).

![Figure 2. Force measurement platform.](image)
Shown in Figure 3 are ultrasound images of the biceps from a healthy subject, at four different applied forces. As you would expect, the muscle thickness as measured from the bone to the subcutaneous fat-muscle separation layer is highly dependent on force. Such variable compression impacts the quantities extracted from US image analysis, both physical parameters such as elasticity, and image-based parameters (image based biomarkers) such as average gray-scale level or measures of image texture.

![Ultrasound images of the biceps from a healthy subject, at four different forces.](image)

Figure 3. Ultrasound images of the biceps from a healthy subject, at four different forces. The muscle thickness, the height of the yellow boxes, as measured from the bone to the subcutaneous fat-muscle separation layer is highly dependent on force.

### 2.2 Force Control Platform

Automatic force control is one way to address the force variation that results from sonographer or patient motion. We have developed a number of handheld force-controlled systems to enhance commercial ultrasound probes\textsuperscript{3–5}. The probe-patient contact force can be held constant to stabilize the image, swept through a range of forces, or cycled. In a low-bandwidth long-range solution, Figure 4, the mechanical portion of the device consists of a ball screw linear actuator driven by a servo motor, along with a load cell, accelerometer, and limit switches. In another high-bandwidth short-range solution, the mechanical portion is controlled by a voice coil actuator. The software combines force- and position-control strategies. The performance of such systems is assessed in terms of frequency response, range of travel, and in hand-held tracking of real and simulated patient motion. Ergonomic control scheme permits smooth making and breaking of probe-patient contact, and helps the operator keep the probe centered within its range of motion.

![Low-bandwidth long-range force-controlled, handheld ultrasound platform.](image)

Figure 4. Low-bandwidth long-range force-controlled, handheld ultrasound platform.
The force-control systems have broad applications as they can be used throughout the body to enhance imaging of clinically significant biophysical parameters, including tissue elasticity. Acquisition-state controlled, consistent, images could also lead to improved biomarker quantitation in longitudinal studies. In conventional sonography, variation in contact force, position, and orientation make dimensional measurements difficult to precisely reproduce at a later date. For instance, clinicians may not be able to determine whether a near-skin-surface tumor has truly changed dimensions or instead is viewed from a different location (this is where the probe re-localization solutions, discussed next, are also useful), or the tumor has been deformed by increased pressure. Moreover, ultrasound data acquired during force-sweep acquisition can be used to enable low-cost compression based elastography or to control the preload-offset for shear wave elastography measurements. We have used force-controlled platforms to suggest that force-correlated images will facilitate the determination of new quantitative biomarkers for muscle.

2.3 Application of force-control to Duchenne muscular dystrophy (DMD)

Characterized by progressive disability leading to death, DMD remains one of the most common and devastating neuromuscular disorders of childhood\(^6\). DMD is caused by a genetic mutation that generates a complex sequence of events in muscle cells, which eventually undergo fibrosis and are replaced by adipose and connective tissue. Average DMD patient survival is to age 25, although in some cases patients have survived into the forties. Although a variety of promising new treatment strategies are in development, outcome measures for clinical trials remain limited for the most part to a set of functional measures, such as the six-minute walk test\(^7\). While clearly useful, such measures are impacted by unrelated factors, such as mood and effort, and have limited repeatability. To address this and other limitations, magnetic resonance imaging (MRI) is now being investigated as a surrogate measure\(^8\). However, more easily applicable, cost-effective, office-based surrogate measures that provide high repeatability and sensitivity while still correlating strongly with disease status would find wider use in Phase II and possibly in Phase III clinical trials in DMD. Ultrasound based quantification of tissue properties along with other image based biomarkers can provide valuable information for such analysis. The information embedded in acquisition-state-controlled US images may provide convenient, non-invasive, clinically meaningful markers of disease progression in DMD that surpass the functional measures currently in use.

Figure 5. Variable compression impacts the quantities extracted from US image analysis, both physical parameters such as elasticity, and image-based parameters such as average gray-scale level or measures of image texture such as edges. Here we show ultrasound B-mode images of control and DMD patient shown with their corresponding binary edge maps, both acquired at 2 Newtons of controlled applied-force.
We are developing clinically meaningful markers of disease progression in Duchenne muscular dystrophy (DMD). We have demonstrated the potential for force-correlated ultrasound imaging to enable automated classification of muscle tissues structures in individuals with Duchenne Muscular Dystrophy. Image-based quantities, such as variance maps, and image texture have been used in classification schemes. We demonstrated that automated classification was improved when the biomarkers extracted – from the quadriceps, biceps, forearm, tibialis anterior, and medial gastrocnemius - were tagged with force information. Similar methods may be used to promote ultrasound as a quantitative non-invasive tool for not only classifying versus a control but also for tracking progression of DMD over time.

2.4 Force variation in elastography

Ultrasound elastography has been a major innovation in the last two decades in medical imaging. It can measure tissue mechanical properties and provide adjunctive information to increase diagnostic confidence. The blooming of this field can be attributed to two main facts: first, the contrast between normal and abnormal pathological tissue is higher in viscoelasticity. Second, tissue viscoelastic property is fundamentally different to the biophysical properties mapped by conventional imaging modalities, such as echogenicity measured by general ultrasound, radio-density in CT, or T1 and T2 relaxation times in MRI. Since the conception of ultrasound elastography, numerous clinical studies have demonstrated its extensive potential in the fields of diagnostics and monitoring, including cancer detection (breast, liver, thyroid, prostate, etc.), tissue characterization (liver and renal fibrosis staging, vascular wall compliance, myocardium contractility), and therapy monitoring and assessment (e.g. liver cancer treatment by HIFU and RFA). Some clinical applications are presently not possible with other imaging modalities. All major ultrasound manufactures in the world have ultrasound elastography - strain and/or shear wave elastography (SWE) - commercially available on their fully-functional diagnostic systems.

Current elastography technology has limitations. Diagnostic ultrasound is an operator dependent medical modality. Naturally, elastography built upon ultrasound, whether strain elastography or SWE, inherits this characteristic. As ultrasound elastography products became more available on the market, clinicians have begun to apply this modality into various clinical applications and examine its potential benefits and limitations. A number of limitations have been identified by scientists and clinicians in the context of technique performance, clinical utility and work-flow. The most frequently acknowledged limitation is repeatability and reproducibility. A few confounding factors introduce bias and variation in stiffness measurement, including operator dependence, concerning both strain elastography and SWE, and cross-vendor system dependence of SWE caused by different shear wave excitation mechanisms, tissue mechanical models and signal processing involved in stiffness reconstruction. Before ultrasound elastography can be fully adopted as a routinely used clinical tool for diagnosis and therapy monitoring, these technical and clinical challenges must be overcome by the entire industry.

Figure 6. The results show significant variation in shear wave elastography estimates of tissue Young’s modulus as a function of preload differences typical of clinical sonography. The varying preload conditions depicted are typical of those seen across a range of operators in routine abdominal sonography and the resultant change in estimated tissue Young’s. This variation is explained by the observation that different bias compression levels pre-strain the tissue to different operating points along the tissue’s non-linear stress-strain response. Estimated Young’s modulus increases from 21.1 to 64.1 kPa in the vastus medialis as applied force (preload) increases from 1 to 18 N.
Soft tissue is mechanically nonlinear, meaning that elastography measurement varies with the operator-applied transducer force (termed preload). Preload-induced variation may lead to inaccurate diagnosis and poses challenges to establishing measurement standardization and clinical guidelines. Even with SWE, which is considered more operator-independent than strain elastography, stiffness measurement on the same tissue can vary significantly. The results in Figure 6 show significant variation in shear wave elastography estimates of tissue elasticity as a function of preload differences typical of clinical sonography. The varying preload conditions depicted, 1N to 18 N, are typical of those seen across a range of operators in routine sonography and the resultant change in estimated tissue Young’s ranged from 21.1 kPa to 64.1 kPa in the vastus medialis. This variation is explained by the observation that different bias compression levels pre-strain the tissue to different operating points along the tissue’s non-linear stress-strain response.

2.5 BP estimation, from an expanded model of compression elasticity

In compression based strain elastography, the displacement vector (or just its vertical component) for each location is estimated by tracking tissue motion using ultrasound signals (RF data, or B-mode). Under the simplifying assumption that the motion of each locality is vertical, the local relative stiffness (strain) is then roughly proportional to the vertical derivative of the vertical component of the displacement. More elaborate estimation using finite-element techniques can give a better estimate of the strain as well as the direct estimation of the elasticity. Crucially, given the capabilities of the of the force-control hardware setup to measure/maintain the exact applied force for different images in the input pair/sequence, this estimation can be made quantitative rather than qualitative (i.e. absolute values of the Young modulus rather than relative distribution of elasticity in the body can be potentially computed). We have started to extend compression elastography to the problem of arterial blood pressure (ABP) calibration and time-varying vessel properties. In this approach, we acquire ultrasound image sequences as a function of applied contact force. From the acquired image sequences, we compute the gradient of the displacement distribution, which forms the approximate tissue strain map. Given the known, controlled contact force at the body surface, the inverse elastography problem can be solved iteratively to determine tissue elasticity as a function of location. We have applied this approach to simultaneously calculating the elastic properties of tissue and the pressure of an enclosed artery, and have established feasibility in simulations and in a realistic phantom set-up.

Figure 7. Skin features includes moles, follicles, and micro-reliefs.

3. POSITION AND ORIENTATION VARIATION

3.1 Skin as a body position encoding system

Patterns of skin features, if looking at a sufficiently large patch of skin - including micro reliefs, follicles, moles, and melanin variation, Figure 7 - are unique. This uniqueness suggests that skin could be used as a relative-motion or absolute-
location encoding system for the body. Based on this observation, we have developed a freehand ultrasound platform, which localizes an ultrasound probe in 6-DOF with respect to the patient (and not room coordinates) by tracking natural skin features (i.e. fiducial-free) with a small camera mounted to the ultrasound probe\textsuperscript{14–16}. The system comprises: (1) an optical camera kinematically coupled to an US transducer, Figure 8, (2) software that extracts unique skin features, and (3) software that localizes the transducer by tracking the skin features\textsuperscript{14–17}.

We simultaneously record, synchronously in time, an ultrasound probe image inside the body and the camera image of the skin. We use skin features to track relative motion along the body. The same skin features can be used to virtually identify and tag unique locations on the body; this system permits placement of the ultrasound transducer in the same body location and orientation by different operators on serial examinations. The skin features used for optical tracking mainly result from uneven distribution of melanin and hemoglobin pigments, pores, and skin surface texture. These features are automatically detected and feature descriptors are computed using the scale-invariant feature transform (SIFT) method\textsuperscript{18}. In practice, multiple sources of information, e.g. camera images and ultrasound images, are then combined for optimal probe pose estimation. In this way, a body-contoured skin map is constructed and each US image is accurately localized with respect to the map - a process termed simultaneous localization and mapping (SLAM)\textsuperscript{19}. In addition, regularities in US images and motion smoothness are considered to further improve the pose estimation.

![Camera based probe position tracking](image)

Figure 8. Camera based probe position tracking (a) hardware design and (b) typical scanning types.

We generate a spatially accurate three-dimensional data set from a standard optically tracked two-dimensional sonogram; using this system we are able to approximately register/re-locate an US probe on patient’s body at a known location and orientation as separate instances in time with respect to patient coordinates and not room coordinates\textsuperscript{14–16}. The 3D data set could be used to generate multi-planar images which should be near indistinguishable from directly acquired US images\textsuperscript{17}. This has several implications; sonograms can be re-formatted in any plane, allowing comparison of matched images across serial examinations, and (large-volume) volumetric sonography can be accomplished. The re-registration ability should improve the ability to longitudinally monitor near-surface or fixed location organs or tissue structures. These technologies have potential application for both low cost 3-D and in high-end systems - such as extended field of view for large volume organs. We validated\textsuperscript{17} volume construction performance on several body parts of multiple human subjects, Figure 9.
3.2 Prosthetics

Finally, we have expanded on the concept of measuring and controlling the imaging acquisition state to the area of US tomography for limb imaging. Demand is increasing for clinical applications of musculoskeletal (MSK) ultrasound, particularly for rehabilitative applications. MSK US shows significant promise as a means to image and collect quantitative data of an individual’s limb and demonstrates distinct advantages as compared to X-rays, CT and MRI. Ultrasound imaging can be used in certain patients that are contraindicated for other imaging modalities and lacks radiation risk.

Multiple research groups have pursued volumetric ultrasound imaging of limbs with varying levels of success. Several systems have been developed for three-dimensional images of the residual limb of amputees. Improved ergonomics, ease of use, and simplified mechanical configuration are necessary to advance such systems to routine clinical practice. Limb motion is difficult to compensate for and degrades image resolution. In previously developed systems, motion compensation for image registration was completed exclusively through matching common image features. Feature matching has proven to be an ineffective approach, however, since shared anatomical structures may appear dissimilar in ultrasound images when collected at various ultrasound probe orientations.

We are developing ultrasound limb imaging systems that address some of these design challenges. Full lower-extremity imaging is performed with a clinical ultrasound probe and camera(s) in a water tank, Figure 10; image registration algorithms compensate for limb motion during scanning.

Our several prototypes have further demonstrated a multi-modal imaging approach for acquiring acquisition state information during ultrasound imaging. Building on our motion tracking results, we have improved automated data acquisition process and improved the optical tracking techniques. A 3D camera is used to acquire a 3D surface as well as provide quantitative information about the location in space of the limb being imaged during the scanning procedure. This information is used to register and stitch the images together into a final compound ultrasound slice or volume, Figure 10.
4. CONCLUSION

In this keynote talk we reviewed several acquisition-state controlled quantitative ultrasound technologies which provide control, measurement, and visibility into the ultrasound imaging process; we highlighted increased quantitative information available from such image(s); and we briefly highlighted the clinical utility of these technologies. Through novel device design, real-time image analysis and machine intelligence, understanding of diagnostic techniques, and system design we work to improve the usability, diagnostic capability, and workflow productivity of ultrasound imaging.

We work to engineer systems that address the major sources of variability in sonography. Significant research is still required to integrate these technologies into systems useable by non-radiologist healthcare professionals. We work to further develop, refine, and validate analysis algorithms and workflow software (along with improvement to the hardware technologies) to produce automated, or augmented, quantitative analysis of ultrasound imagery.

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