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Volumetric Ultrasound and Computer-Assisted Analysis At The *Point-of-Care*: A Musculoskeletal Exemplar

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Abstract— **In this paper we motivate the hypothesis that the use of volumetric ultrasound imaging and automated image analysis tools would improve clinical workflows as well as outcomes at the *point-of-care*. To make our case, this paper presents results from a rheumatoid arthritis (RA) study [1] where several image analysis techniques have been applied to volumetric ultrasound, highlighting anatomy of interest to better understand disease progression. Pathologies related to RA in joints, manifest themselves commonly as changes in the bone (e.g. erosions) and the region enclosed by the joint-capsule (e.g. synovitis). Automated tools for detecting and segmenting such structures would help significantly towards objective and quantitative assessment of RA in joints. Extracted bone coupled with a simple anatomical model of the joint provides a coarse localization of the joint-capsule region. A probabilistic speckle model is then used to iteratively refine the capsule segmentation. We illustrate the performance of proposed algorithms through quantitative comparisons with expert annotations as well as qualitative results on over 30 scans obtained from 11 subjects.**

I. INTRODUCTION

Conventional 2D ultrasound is a real-time medical imaging modality that creates cross-sectional images of soft tissue by sending and receiving ultrasound waves from a transducer (also called a probe). Images are formed by the amplitude and timing of the returned echoes, assuming a constant sound velocity in tissue. In order for the sound waves to couple into the tissue, a coupling gel is used and this must be free of air bubbles to avoid artifacts. Other sources of artifacts can include refraction from tissue interfaces that are parallel to the normal from the probe face, which results in shadowing and other distortions in the image. The operator of the ultrasound equipment must manipulate the probe to obtain the optimal image based upon their subjective judgment of image quality during the examination. Since the operator can see the real-time images, they can perform this search dynamically, but they must understand how to obtain the best image of the anatomy they are examining. This requires the operator to be skilled in the use of ultrasound and to have a detailed understanding of the expected image quality for specific anatomy, both of which take considerable training in order to master. Skilled sonographers are capable of obtaining relevant images of a wide variety of anatomy with years of experience, but are often focused on specific examinations, such as womens health, cardiac/cardiovascular, or abdominal imaging. Many clinicians are not skilled in obtaining or interpreting ultrasound images and thus must refer patients that need ultrasound exams for a separate ultrasound consultation, adding to the cost of healthcare and delays in treatment. Barriers to the use of ultrasound include questionable reproducibility based upon the subjective manipulation by the operator, complex interpretation of the anatomy presented by 2D ultrasound that may not reflect the 3D anatomical reality, the requirement of extensive experience to use the equipment and interpret ultrasound images, and a lack of quantification tools in most applications. Our hypothesis is we can significantly lower the barriers to ultrasound imaging for most clinicians by using volumetric ultrasound and advanced image analysis tools to provide intuitive visualization, automatically highlighting specific anatomy of interest based upon objective parameters and the possibility of quantification for enhanced understanding of disease progression or response to therapy. In this direction, this paper presents results from a rheumatoid arthritis study [1] where several image analysis techniques have been applied to volumetric ultrasound, highlighting anatomy of interest to better understand disease progression.

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II. MUSCULOSKELETAL APPLICATION: RHEUMATOID ARTHRITIS

A. Clinical Background

Arthritis and other rheumatic conditions are the leading cause of disability in the United States, making it a major public health problem [14]. Arthritis, including rheumatoid arthritis and gout, is one of the most common chronic diseases in the United States. Forty-six million Americans (or one out of every five adults) have arthritis diagnosed by a physician, and 300,000 children have arthritis [14]. Consequently, arthritis poses a large clinical burden, with 36 million ambulatory visits and 750,000 hospitalizations [14]. In most populations, rheumatoid arthritis has a prevalence of about 1%, women being affected twice as often as men. This would mean that at least 3 million people in the United States and 68 million worldwide were affected by rheumatoid arthritis.

Currently, for the assessment of rheumatoid arthritis, rheumatologists rely largely on indirect measures of disease activity, such as external clinical examination or the assessment of indirect markers of inflammation such as sedimentation rate or measurement of C-reactive protein. These may or may not reflect inflammatory activity at the joint level. Conventional (X-ray) Radiography (CR) can demonstrate erosions in rheumatoid arthritis. However, CR projects three-dimensional structures on a two-dimensional plane, whereby bony tissues are superimposed on each other in the X-ray image. Erosions can therefore only be diagnosed if the erosion is seen in profile as a break in the bony cortex. For this reason, cross-sectional imaging including ultrasound can detect more erosions in rheumatoid arthritis than CR [16]. Cross-sections of tissues can also be obtained in several planes using Magnetic Resonance Imaging (MRI), which allows approximated assessment of volumes of diseased structures. However, the precision of such measurements is limited by the resolution of MRI images and by considerable cost which prohibits serial imaging in a given patient. Some patients affected by arthritis also cannot undergo MRI scanning because of implanted devices, claustrophobia, etc. These disadvantages can potentially be overcome with the use of an alternate imaging modality, *Ultrasound*, that has been used to assess common forms of inflammatory arthritis including rheumatoid arthritis and gout [17]. Moreover, in contrast with other cross-sectional imaging modalities including MRI and CT scanning, Ultrasound is safe, inexpensive, and is widely available worldwide. High frequency ultrasound is particularly suited to assess superficial tissue structures including tendons and joints.

B. Challenges

Using conventional 2D ultrasound, rheumatologists can reach good to very good agreement on findings, if they are well trained and follow a standardized examination protocol [15]. Nevertheless, most rheumatologists who perform musculoskeletal (MSK) ultrasound have very limited experience in use of sophisticated Ultrasound systems. This may be particularly true in the United States, where the first ultrasound courses for rheumatologists were not introduced until 2005. Dependence on the skill of the operator is therefore frequently noted as an impediment to more widespread use of MSK ultrasound. The operator dependence of 2D ultrasound also makes it very challenging to assess disease progression and response to treatment over time, which is critical for treatment planning as well as developing drugs. If ultrasound is integrated in clinical practice, time constraints are another factor that complicates acceptance. Thus, though ultrasound is known to be very helpful in assessing rheumatoid arthritis, its utility at the point of care has been limited. It is therefore desirable to develop and utilize dedicated technologies (hardware and software) that alleviate these obstacles, thereby providing faster and more accurate diagnosis and assessment of treatment response. Ideally such technology would enable greater ease of use, shorter learning period, faster exam time, and reduce operator dependence.

Clinical research has shown that volumetric (3D) ultrasound is more sensitive to pathologies like erosion [15], [16] than 2D ultrasound. Moreover, volumetric quantification of arthritis related anatomical structures (e.g. bony erosions, hypertrophic synovium, etc) would add considerable value to the information provided by the ultrasound system to the rheumatologist towards precisely assessing the disease and deciding treatment plans. Hence, one of the main objectives of this work is to develop advanced automated image analysis algorithms for volumetric (3D) ultrasound specifically to be used in rheumatological practice. This would enable automatic extraction of clinically relevant volumetric information from the ultrasound images in real-time and at the same time reduce operator dependence of ultrasound based clinical assessment of rheumatoid arthritis. Such technology, if successful, would allow rheumatologists to arrive at precise diagnoses at the point-of-care and in a short period of time within the framework of a regular office visit.

Currently, in the absence of such tools, patients are routinely referred to a radiologists office for further diagnostic imaging, which increases costs and delays patient care. If we can use automated measurements obtained from a volumetric probe and image analysis algorithms to help the rheumatologist arrive at a diagnosis during a regular office visit, these findings can be discussed with the patient at the point of care, and an informed decision regarding treatment plan can be reached without delay. Healthcare expenditures related to rheumatoid arthritis would also see an overall decrease, if repeated use of expensive imaging modalities including CT scanning and MRI scanning can be minimized. It has been shown that early treatment decreases later disability in rheumatoid arthritis [14], so we believe that societal costs due to the disease burden of rheumatoid arthritis would decrease, if improved diagnostics leads to consequent appropriate treatment.

C. Data

In order to generate preliminary data towards motivating the use of volumetric ultrasound, thirty-one (31) 3D datasets of 11 joints in 9 subjects were obtained (rheumatic disease: $n = 6$). High frequency 3D US equipment was used (Voluson-i and RSP-6-16 probe, GE Healthcare, Wauwatosa, WI). Joints examined included metatarsophalangeal (MTP) joints, $n = 3$; metacarpophalangeal (MCP) joints, $n = 6$; proximal interphalangeal (PIP) joint, $n = 1$; and a shoulder joint, $n = 1$. All US studies were performed by a rheumatologist certified in musculoskeletal US, with 20 years of US experience (RT). An example ultrasound image is shown in Figure 1. One can observe that the joint capsule region is not uniform across 2D slices and hence looking at a true 3D rendering as in Figure 2 would provide more information. The following sonographic features, relevant to rheumatology, were examined:

- Bony contour to assess erosions, and to determine the bony surface of the joint as an anatomic landmark, or starting point, for the assessment of synovitis.
- Joint capsule to determine normal versus distended joint cavity
- Volume of proliferative synovial tissue

D. Automated Analysis - Preliminary Results

In [1], we proposed to improve and extend to 3D the method presented in [2] for bone extraction in 2D images using a dynamic programming approach. As suggested in [11], we utilized the basic physical principles of US imaging coupled with information of the scanning geometry to automatically extract the bone surface from the 3D scan of a joint. After extracting the bone surface, we then utilized a simple anatomical

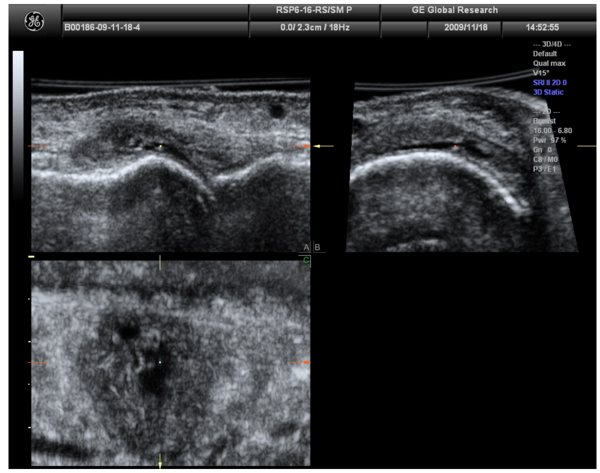

Fig. 1. Illustration of a typical "tri-plane" view obtained from a volumetric ultrasound scan.

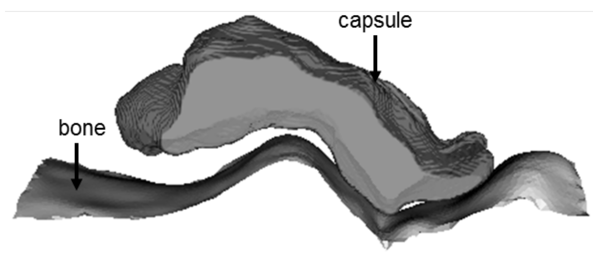

Fig. 2. 3D rendering of the bone surface and joint-capsule region extracted using our proposed algorithms in [1].

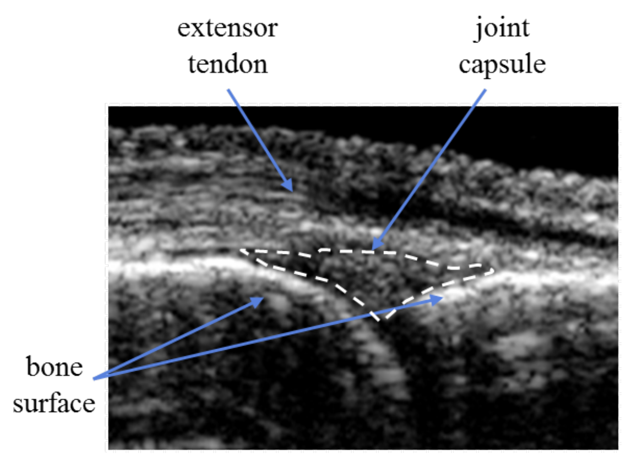

Fig. 3. Sonographically observed anatomy of a Metacarpophalangeal (MCP) joint (derived from [10]).

model of the metacarpophalangeal (MCP) joints [10] (see Figure 3) to automatically segment the joint capsule region which lies between the bones forming a joint. A qualitative (visual) inspection of implementing the proposed bone-surface detection algorithm on all the datasets led to very encouraging results as indicated in Table I.

TABLE I
SUMMARY OF DATA AND QUALITATIVE (VISUAL) EXPERT-ASSESSMENT OF BONE-SURFACE EXTRACTION RESULTS.

Joint	Joint No.	Datasets	Qualitative Accuracy
MCP	6	18	95%
MTP	3	9	90%
PIP	1	2	85%
Shoulder	1	2	100%

Figure 4 shows the extracted bone surface contours from representative slices of some 3D volumes. We applied the proposed bone-extraction method to over 30 volumes of different joints from 11 subjects. For a quantitative validation, we used expert[1] annotation of randomly selected 2D slices from 7 of the 3D volumes to compare our results (approximately 5 slices per volume). The expert annotations (red overlay) and corresponding detections (green-overlay) can be qualitatively evaluated from Figure 4 (yellow overlay indicates exact match between reference and the automated algorithm). The maximum average distance of the extracted bone with respect to the expert labelling was 0.3mm (approximately 1-2 voxels). For a detection tolerance of 1mm, we observed maximum false-positive (FP) and false-negative (FN) rates of 1.2% and 1.4% respectively, with a maximum and minimum detection rate (DR) of 98.3% and 82.8% respectively.[2] Figure 5 shows the initial seed (left-column) using our simple anatomical prior and the final segmentation based on probabilistic speckle modelling (right-column). Again, for quantitative validation we used expert annotation from representative slices containing the joint capsule. The proposed algorithm achieved average precision and recall rates of about 87% and 80% respectively. Our algorithms were implemented using experimental non-optimized code leveraging the Insight Toolkit (ITK) library in C++. The bone extraction as well as capsule segmentation took approximately 5 minutes for a 200x100x100 size volume on a laptop with an Intel© i5 processor and 4GB of RAM.

[1]Over 25 years of experience with musculoskeletal US.

[2]These statistics (average, maximum, minimum) are computed over the evaluation results from all 7 labelled datasets.

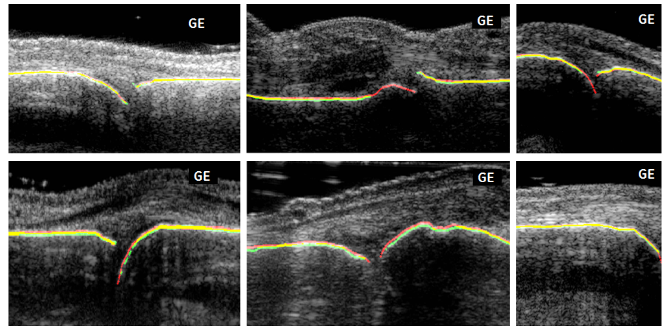

Fig. 4. A collage of 2D slices from 3D bone-extraction results on scans from multiple subjects. Expert annotations (red) and detections (green) are overlaid. Yellow overlay indicates a perfect match between the two.

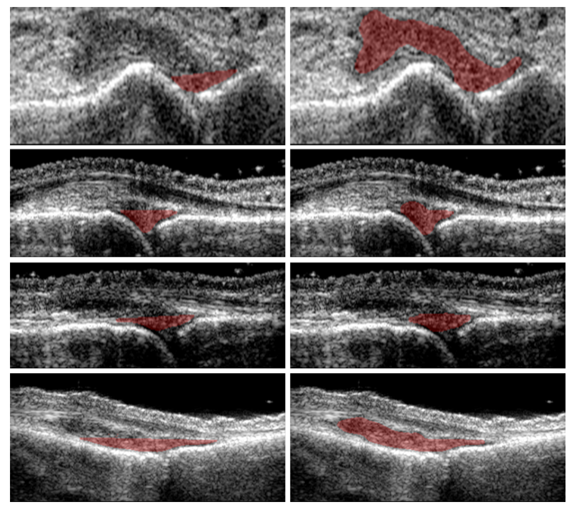

Fig. 5. Capsule segmentation results from multiple subjects. Initial seeds (left-column) and final segmentation (right-column).

III. DISCUSSION

We strongly believe that the use of volumetric ultrasound imaging and automated image analysis tools would improve clinical workflows as well as outcomes at the *point-of-care*. Towards making our case we provide the exemplar of a recent rheumatoid arthritis study, where using image analysis algorithms, we have shown successful segmentation of both bony surfaces and joint capsules in a rheumatoid arthritis study. The results from the algorithm were compared to manual identification of these features by an expert ultrasound interpreter and the algorithm was shown to be accurate. Once these features have been identified, there are several other disease specific features that can be quantified as needed, including joint capsule distension by comparing normal joint volumes to those in cases of rheumatic disease, echogenicity within the joint capsule as an indicator of tissue proliferation, and blood flow in the joint capsule (hyperemia). The bony surface can also be used for longitudinal studies in order to co-register images and track disease progression or response to therapy. Additional work is needed to show the clinical significance of these techniques, but this paper has shown the feasibility of automatically detecting these key features towards objective assessment of rheumatic disease.

REFERENCES

[1] K. Patwardhan, K. Cao, D. M. Mills, and R. Thiele, "Automated Bone and Joint-Region Segmentation in Volumetric Ultrasound," *Accepted for presentation at IEEE International Symposium on Biomedical Imaging*, May 2012.

[2] P. Foroughi, E. Boctor, M. J. Swartz, R. H. Taylor, and G. Fichtinger, "Ultrasound bone segmentation using dynamic programming," in *Proc. IEEE Ultrasonics Symp*, 2007, pp. 2523–2526.

[3] R. J. Wakefield, W. W. Gibbon, P. G. Conaghan, P. O'Connor, D. McGonagle, C. Pease, M. J. Green, D. J. Veale, J. D. Isaacs, and P. Emery, "The value of sonography in the detection of bone erosions in patients with rheumatoid arthritis: a comparison with conventional radiography.," *Arthritis Rheum*, vol. 43, no. 12, pp. 2762–2770, Dec 2000.

[4] M. Backhaus, G. R. Burmester, D. Sandrock, D. Loreck, D. Hess, A. Scholz, S. Blind, B. Hamm, and M. Bollow, "Prospective two year follow up study comparing novel and conventional imaging procedures in patients with arthritic finger joints.," *Ann Rheum Dis*, vol. 61, no. 10, pp. 895–904, Oct 2002.

[5] U. M. Döhn et al, "Are bone erosions detected by magnetic resonance imaging and ultrasonography true erosions? a comparison with computed tomography in rheumatoid arthritis metacarpophalangeal joints.," *Arthritis Res Ther*, vol. 8, no. 4, pp. R110, 2006.

[6] I. Hacihaliloglu, R. Abugharbieh, A. J. Hodgson, and R. N. Rohling, "Enhancement of bone surface visualization from 3D ultrasound based on local phase information," in *Proc. IEEE Ultrasonics Symp*, 2006, pp. 21–24.

[7] L. Lopez-Perez, J. Lemaitre, A. Alfiansyah, and M. Bellemare, "Bone surface reconstruction using localized freehand ultrasound imaging," in *Proc. 30th Annual Int. Conf. of the IEEE Engineering in Medicine and Biology Society EMBS 2008*, 2008, pp. 2964–2967.

[8] H. Overhoff and D. Lazovic, "Visualization of the newborn's hip joint using 3-d ultrasound and automatic image processing," 1999.

[9] Y. Zhang, R. Rohling, and D. K. Pai, "Direct surface extraction from 3d freehand ultrasound images," in *Proc. IEEE Visualization VIS 2002*, 2002, pp. 45–52.

[10] N. Boutry, A. Lard, X. Demondion, B. Cortet, H. Cotten, and A. Cotten, "Metacarpophalangeal joints at us in asymptomatic volunteers and cadaveric specimens.," *Radiology*, vol. 232, no. 3, pp. 716–724, Sep 2004.

[11] J. A. Noble and D. Boukerroui, "Ultrasound image segmentation: a survey," vol. 25, no. 8, pp. 987–1010, 2006.

[12] Z. Wang, G. Slabaugh, G. Unal, and T. Fang, "Registration of ultrasound images using an information-theoretic feature detector," in *Proc. 4th IEEE Int. Symp. Biomedical Imaging: From Nano to Macro ISBI 2007*, 2007, pp. 736–739.

[13] X. Han, Xu. C., and J. L. Prince, "A topology preserving level set method for geometric deformable models," vol. 25, no. 6, pp. 755–768, 2003.

[14] `http://www.cdc.gov/arthritis/basics/rheumatoid.htm`

[15] M. Backhaus, G. R. Burmester, D. Sandrock, et al. "Prospective two year follow up study comparing novel and conventional imaging procedures in patients with arthritic finger joints." in *Annals of the Rheumatic Diseases* 2002;61(10):895-904.

[16] B. J. Ejbjerg, M. Court-payen, M. Hasselquist, et al. "Are bone erosions detected by magnetic resonance imaging and ultrasonography true erosions? A comparison with computed tomography." in *Rheumatoid Arthritis Metacarpophalangeal Joints* 2006;8(4):1-9.

[17] R. G. Thiele, N. Schlesinger "Diagnosis of gout by ultrasound." in *Journal of Laboratory and Clinical Medicine* December 2006, pp: 1116-1121.

[18] A. K. Scheel, K. A. Hermann, E. Kahler, et al. "A novel ultrasonographic synovitis scoring system suitable for analyzing finger joint inflammation in rheumatoid arthritis." in *Arthritis and Rheumatism.* 2005;52(3):733-43.