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Abstract: Ultrasound image segmentation deals with delineating the boundaries of structures, as a step towards semi-automated or fully automated measurement of dimensions or for characterizing tissue regions. Ultrasound tissue characterization (UTC) is driven by knowledge of the physics of ultrasound and its interactions with biological tissue, and has traditionally used signal modelling and analysis to characterize and differentiate between healthy and diseased tissue. Thus, both aim to enhance the capabilities of ultrasound as a quantitative tool in clinical medicine, and the two end goals can be the same, namely to characterize the health of tissue. This article reviews both research topics, and finds that the two fields are becoming more tightly coupled, even though there are key challenges to overcome in each area, influenced by factors such as more open software-based ultrasound system architectures, increased computational power, and advances in imaging transducer design.

Keywords: ultrasound, quantitative ultrasound, ultrasound image segmentation, ultrasound tissue characterization

1 INTRODUCTION

Image segmentation, or the delineation of object boundaries in images, is one of the oldest image analysis problems and has been well studied. Ultrasound imaging is arguably the hardest medical imaging modality upon which to perform segmentation. In early ultrasound image segmentation papers, the quality of data was poor, and image analysis typically meant applying a threshold to the image intensities in an attempt to separate background from foreground. Needless to say, this did not work well. In recent years, the quality of ultrasound images, in terms of signal-to-noise and contrast-to-noise ratio, has increased substantially. This has led to a resurgence of interest in developing methods for automating the delineation of geometric boundaries of objects imaged using ultrasound, and also characterizing tissue properties within these boundaries. This review article attempts to provide a general overview of the state of the art in this area, particularly focusing on soft-tissue applications. A detailed comparison of methodologies and a broad survey of application areas are beyond the scope of the current article but are provided in reference [**1**].

Ultrasound tissue characterization (UTC) is related to the ultrasound image segmentation problem in that the goal of image segmentation is typically (although not exclusively) to delineate the boundaries between tissues that are different in some sense in order to make a size measurement or to characterize the difference between healthy versus diseased. However, as will be seen, most ultrasound image segmentation methods have been developed for B-mode (log-compressed) images, not radio-frequency (RF) signals (unprocessed ultrasound data), largely because B-mode images are the ones traditionally available on commercial ultrasound systems.

The traditional goal in UTC is to use ultrasound modelling and signal analysis to derive parameters that can characterize and differentiate between healthy and diseased tissues. Applications abound in the literature and include the classification of tissues in the breast [**2**, **3**], liver [**3**], heart [**4**, **5**], eye [**6**], and skin [**7**]. It is beyond the scope of this review

to discuss all these application areas in detail. For earlier reviews on ultrasound tissue characterization and perspectives, see references [**8**] and [**9**].

2 ULTRASOUND IMAGES

The basic ultrasound image formation process will first be outlined briefly, in order to place in perspective the different classes of image segmentation and ultrasound tissue characterization methods that are to be discussed.

In a standard ultrasound system there are three basic types of data available for analysis: radio-frequency (RF) signals, envelope-detected signals, and B-mode images. A transmit/receive ultrasound transducer receives multiple analogue radio-frequency (RF) signals which are converted to digital RF signals and beam formed into a single RF signal. The RF signal is then filtered, and envelope detection is performed to give an envelope-detected signal. Finally, the envelope-detected signal undergoes log compression, and often proprietary post-processing is applied to give a greyscale representation. The resulting signals are then interpolated and rasterized to give a B-mode or display image.

Commercial ultrasound machines typically provide B-mode images only, which is why most image segmentation work has been published using this form of ultrasound data. The problem with working with B-mode images is that the complete ultrasound image formation process is difficult to model, so effects due to attenuation, speckle, etc. are compounded together. The increased availability of ultrasound research interfaces (for instance, the Sonix RP system (Ultrasonix, Canada) or the Axius Direct™ Ultrasound Research Interface (Siemens Medical Solutions USA, Inc.)) is providing researchers with more control of acquisition parameters, and hence the opportunity to consider segmentation strategies that work further up the processing pipeline (envelope detection and RF signal level). (In reference [**10**], analysis is performed on the in-phase/quadrature (IQ) signal which is obtained by demodulating the RF signal.) Ultrasound tissue characterization, on the other hand, is most often done on the RF signal or envelope-detected signal.

3 IMAGE SEGMENTATION

Ultrasound image segmentation is largely driven by the clinical need to delineate boundaries in B-mode images as a step towards dimension measurement of anatomy or sizing of disease extent. However, ultrasound B-mode imaging is not always suitable for anatomical imaging. In particular, B-mode imaging is often compared with other clinical imaging modalities, particularly (X-ray) computer tomography (CT) and magnetic resonance imaging (MRI), and criticized for its poor signal-to-noise ratio and 'noisy' appearance. Conventional image analysis methods that have been found to work well on CT and MRI images often do poorly if applied to ultrasound images, as they assume good boundary definition (strong-intensity edges). The appearance of geometric boundaries of objects imaged using B-mode ultrasound is dependent on the acoustic impedance difference between materials and on other factors including the insonification angle, attenuation, signal drop-out, etc. This has three important implications for image segmentation, particularly when the goal is to provide automated image measurement. First, there are often partially missing boundaries, which means that computer algorithms have to 'fill in' the missing information somehow. Second, the acoustic impedance (perceived) boundary in a B-mode ultrasound image may not necessarily delineate the tissue–tissue interface of interest. For instance, in breast cancer ultrasound imaging, B-mode ultrasound imaging sizing underestimates the true cancer size. Third, owing to the nature of ultrasound B-mode image reconstruction, a speed of sound of 1540 m/s is assumed in all soft tissue. Errors in sizing measurements will result if the true speed of sound in a material differs significantly from this [**11**].

A second important consideration in ultrasound image segmentation is how to deal with speckle. Speckle gives ultrasound images their granular texture appearance. It is formed from backscattered echoes of either randomly or coherently distributed scatterers in tissue, and is a well-studied phenomenon in both ultrasound and other types of coherent imaging such as laser imaging and synthetic aperture radar (SAR) imaging. The statistical properties of the received echo signal have been shown to depend on the density and spatial distribution of scatterers [**12**]. For the case of *fully developed* speckle, when there are a large number of randomly located scatterers, the statistics of the received envelope signal follow a Rayleigh distribution [**12**]. In the case of *partially developed* speckle, where there is a low effective scatterer density, the *K*-distribution is an appropriate model [**13**], and when there is a coherent component that might, for instance, account for regular structures in tissue, the Rice

distribution is appropriate [**12**]. Generalizations, including the generalized *K*-distribution, the homodyned *K*-distribution [**14**], and the Rician inverse of Gaussian distribution [**15**], have been proposed to account for different scatterer conditions, but their forms are analytically complex. Simpler general models, in particular the Nakagami family [**16**], have been proposed and have gained some popularity in the segmentation and tissue classification literature (see, for example, references [**13**] and [**18**] to [**22**]). Brusseau *et al.* [**17**], for instance, argues that, for intravascular ultrasound imaging (IVUS), a Rayleigh distribution is a good first approximation. For a comparison of models assessed for use in echocardiographic image segmentation, see the recent paper by Nillesen *et al.* [**5**]. Empirical models of speckle in clinical (display) B-mode images have also been proposed. For instance, a recent paper by Tao *et al.* [**23**] has compared the validity of the gamma, Weibull, normal, and log-normal distributions on clinical cardiac images acquired from machines with different settings.

The choice of automated or semi-automated image segmentation method depends on the task in question, for example detection of an object, accurate sizing, or object tracking. The choice also depends on the quality of data, although in practice the latter has often been ignored, with most methods of ultrasound image segmentation applied only to good-quality data, i.e. subjects with a good acoustic window. As methods are starting to be used more in a clinical setting, characterization of the performance of methods, at least on a range of image qualities, is starting to appear in the literature and is likely to be an important area of research in coming years.

The focus here is mainly on B-mode display image segmentation, and two-dimensional (2D) segmentation will be assumed unless otherwise stated. As described in reference [**1**], a good way to characterize an ultrasound image segmentation method is in terms of the constraints (or prior knowledge) that can be utilized to find a solution to the segmentation problem in hand. Here, the key constraints will be summarized, and a non-exhaustive list of papers illustrating the different concepts will be provided.

A first class of four constraints relates to information that can be extracted from the image data:

1. *Grey level distribution*. A number of empirical grey level distribution models have been employed, including the Gaussian (primarily owing to its ease of implementation), exponential, gamma, beta Weibull, and log-normal distributions, as noted earlier. The Rayleigh model of speckle has also proven popular but is applicable to the envelope signal and not to display B-mode imaging, which is a post-processed version of the envelope signal. A grey level distribution constraint works well in characterizing region characteristics but ignores effects such as signal attenuation, shadowing, and signal drop-out.
2. *Intensity derivatives*. As in other areas of image analysis, the intensity gradient has proved to be a very popular measure to use, as an extremum in the intensity gradient localizes a 'step' change in intensity [**24**–**27**]. It thus works well when there is a strong acoustic boundary between different tissues or (say) the blood pool and tissue, but, because of the anisotropy of ultrasound image acquisition, closed boundaries of real objects often have missing 'edges'.
3. *Local image phase*. Some research groups, including the present author's group, have argued that local image phase is more robust than intensity gradient for acoustic boundary detection [**28**–**30**]. Local phase is estimated using quadrature filter banks and can be readily extended to *N* dimensions using the monogenic signal representation.
4. *Image texture*. Generalized statistical texture analysis methods, such as co-occurrence matrices [**31**], have been shown to characterize image regions for classification purposes and have been utilized in segmentation methods with some success [**32**–**36**], as have wavelets [**37**]. However, image texture is intrinsically a function of the microstructure of tissue and the imaging system, with different system parameters leading to different texture patterns. Thus, it does not provide a true characterization of physical properties of tissue. Image texture characterization is also strongly dependent on the chosen spatial scale of analysis, and therefore should really be considered using a multiresolution approach.

A second class of constraints (5 and 6 below) is a function of the subject or application rather than the imaging modality:

5. *Shape*. This may simply take the form of insisting that the segmentation has a smooth boundary, using an explicit shape representation such as a point distribution model [**38**] within an active shape model framework, or an implicit shape representation such as a signed distance transform [**39**]. Lin *et al.* [**40**] proposed to use propagation of shape across multiresolutions, which is a weak form of shape constraint.

6. *Motion*. Given that ultrasound imaging is often used because it provides dynamic images, the literature on motion-based segmentation and tracking is large [**1**]. Again, the segmentation solution may simply require that the solution be globally or locally smooth, i.e. have temporal coherence (for example, reference [**24**]). The solution may assume a parametric model of motion, such as constant velocity (for example, reference [**41**]), or time may be explicitly included in the segmentation optimization (for example, reference [**42**]).

There are a number of general image segmentation frameworks that have evolved over the last two decades that can combine two or more of the above six constraints, the most popular of which are those based on energy minimization, most commonly called the 'snakes' approach [**43**], and those based on level-set front propagation [**44**] (also, see reference [**45**] for a recent review on region-based level-set approaches). There are many examples in the ultrasound image segmentation literature that are based on these principles. Some examples are listed below, indicating in parentheses the principal prior knowledge utilized:

(a) snakes – [**46**] (4, 5), [**24**] (2, 6), [**32**] (4, 5), [**47**] (2, 6), [**48**] (1, 5);
(b) level sets – [**40**] (2, 5), [**49**] (4, 5), [**50**] (2), [**51**] (2), [**52**] (1, 5, 6).

Note that a number of these methods use preprocessing steps to reduce speckle which will influence performance, etc.; for instance, in reference [**51**] a cubic spline was fitted to the edges after segmentation.

Both the snakes and level-set methodologies are iterative optimization methods that typically require a good initialization to prevent the solution getting stuck in a local minimum. The weighting of the different terms (which trades off the importance of each term) in the functional is typically determined by experimentation and can be an 'art'. The attraction of these methods is that they are relatively simple to implement, and, in 2D at least, they are relatively quick to execute on standard PC computers. They generally work better on good-quality data.

Other *shape-based* approaches include both those based on fitting deformable models, an approach that works well when parametric shape fitting provides a good first approximation for volume estimation (as used, for instance, in segmenting the prostate [**25**]), and those that use active shape and appearance models, where the expected shape and appearance of an object learned from a training set are used to guide segmentation (for example, reference [**42**]).

In the case where constraints 5 and 6 are not applicable, i.e. the only constraints are image based, the best approach to ultrasound image segmentation may be to use a machine-learning approach, where pixel classification is based on a set of input features computed from the image intensities. This may be the case in soft-tissue disease assessment, for instance assessment of tissue damage or detection/characterization of cancer. For example, this approach has been used for breast mass characterization [**34**, **35**, **53**]. Clearly, the success of this method depends on the choice of image feature and quality of data (see also section 4, where RF-based features are discussed).

There are some recently published methods in the ultrasound image segmentation literature that, although arguably still being researched, are mentioned here because they have certain features that make them well suited for ultrasound segmentation, and the general ideas are likely to be around for some years to come.

In some areas of clinical application of ultrasound, for instance fetal ultrasound, large databases of 'similar' images are gathered, and in this case machine-learning-based approaches to ultrasound image segmentation have been recently proposed. Caneirio *et al.* [**54**], for instance, used a large database of expert-annotated fetal ultrasound scans to train a constrained probabilistic boosting tree (PBT) classifier [**55**] to learn the appearance of an image region in which an automated measurement is then made. Note that the definition of segmentation is different to how it was defined previously, and here refers to the problem called *structure detection* in reference [**54**], which is finding an image region in which an image measurement can subsequently be made automatically. Image appearance in this case is defined in terms of Haar wavelets. Their approach was applied to a number of 2D fetal measurement tasks with training databases of 325–1426 samples. The training step is computationally expensive, but measurement on a new example was reported to take under half a second on a standard dual-core PC computer. The probabilistic boosting tree classifier is only one type of discriminative classifier, and others, such as random forests [**56**] – claimed to be of comparable accuracy with boosting but faster – are also being investigated for ultrasound image segmentation [**57**]. Adaboost was used for IVUS characterization in reference [**58**].

Machine-learning approaches are powerful 'black-box' techniques that aim to handle possibly large natural variations in ultrasound image appearance and quality by characterizing 'similarity' using pattern recognition techniques from a large database of examples. They are particularly useful for analysing problems that are difficult to characterize and model explicitly, such as ultrasound image formation. Using the machine-learning paradigm, the assumption is that a new instance (image) can be classified using this training database. If images of varying quality form part of the training set, then in theory this provides one way to make measurements on low-quality data. An alternative idea for segmenting low-quality images is to build a probabilistic atlas from sample training images and to warp this to a new image in an optimization framework, as in the work of Narayanan *et al.* [**59**], which was applied for guiding prostate biopsies. In their work, the probabilistic atlas was derived from ultrasound images, but it could also be derived from another image modality (such as MRI) that has higher anatomical definition than an ultrasound scan. This is actually registration-guided segmentation and is an approach particularly well suited to image-guided interventions and therapy.

The methods above have all been developed for conventional B-mode display images. When RF data are available, there are two further possibilities. If tissue regions can be distinguished by speckle properties, then it is possible to work with the envelope-detected signal and use a region-based segmentation strategy as in references [**11**], [**17**], and [**22**]. Alternatively, it may be possible to obtain a better image segmentation by processing the RF data because of the higher axial spatial resolution and preservation of signal structure. In this case the general idea is to estimate acoustic-based parameters from the RF signal and use this as the basis of either a pixel-based classification method or deformable-model-based segmentation. This will be discussed at the end of section 4.

4 TISSUE CHARACTERIZATION

Ultrasound tissue characterization, as with image segmentation, is a very old and well-studied problem ([**60**] and references therein). The ultimate goal in tissue characterization is to provide a *parametric image* (spatial map) of a tissue property, although, in many cases today, tissue characterization is restricted to a small sample region or a region of interest rather than the generation of a parametric image. Ultrasound tissue characterization is challenging to do because the interactions between biological tissue, which is an inhomogeneous medium, and an acoustic wave is very difficult to model. In particular, factors such as signal attenuation, which is frequency dependent, and beam diffraction, which makes the spatial and spectral beam characteristics depth dependent, affect the estimation of key parameters such as ultrasound backscatter. This has meant that tissue characterization is not always strictly quantitative, but it can be used to distinguish between different tissues. The following discussion will focus on how some of the key parameters are estimated. The physical principles of medical ultrasound that underpin these parameters are described elsewhere in this Special Issue and in books such as that by Hill *et al.* [**11**].

There are a number of established acoustic and tissue parameters in the literature, some of which can be derived from the estimation of the local power spectral density (PSD) of an RF image. These parameters are defined as follows:

1. *Integrated backscatter (IBS) coefficient*. The integrated backscatter coefficient [**61**–**63**] is estimated as

$$\mathrm{IBS} = \sum_{\mathrm{BW}} \mathrm{PSD}(f)$$

   where the power spectral density is estimated from the discrete Fourier transform of a segment of the RF signal, and the summation is performed over the bandwidth BW (normally -20 dB). IBS provides an estimate of the backscattered energy and has been widely used as a tissue characterization measure, as well as in image segmentation.
2. *Mean central frequency (MCF)*. The mean central frequency is the first moment (mean) of the BW of the power spectrum [**62**]

$$\mathrm{MCF} = \frac{\sum_{\mathrm{BW}} f.\mathrm{PSD}(f)}{\mathrm{IBS}}$$

   The measure is related to the attenuation of the signal as attenuation increases with frequency, producing a decay of the spectrum towards low frequencies.
3. *Attenuation coefficient*. The attenuation coefficient of various soft tissues and biological fluids is a function of frequency [**11**], and this has led to interest in using the attenuation coefficient to distinguish between benign and malignant

disease. Characterizing attenuation is also important from a B-mode image quality perspective because, if it can be quantified, then it can be corrected for in order to improve B-mode appearance [**64**].

In theory, the attenuation coefficient can be estimated using time domain [**65**] or frequency domain methods, although frequency domain methods have proved more popular. In the frequency domain there are two fundamental approaches: the spectral shift method [**66**] and the spectral difference method [**67**]. Both require estimation of the power spectrum based over a region of interest, the size of which determines the spatial resolution of attenuation coefficient estimation. The methods also assume that diffraction and refraction can be ignored, and the scatterer type is constant over the region of interest. In practice, spectral shift methods are found to be sensitive to local spectral noise and diffraction effects (system-dependent effects), while spectral difference methods can poorly estimate the attenuation coefficient close to tissue boundaries. To address these limitations, Kim and Varghese [**68**] recently proposed a hybrid method that is shown to perform better than either class of method on tissue-mimicking phantoms. Attempts have also been made to estimate the attenuation coefficient from the envelope of the RF signal [**69**, **70**].

4. *Speed of sound*. The mean speed of sound in biological tissue is normally assumed to be 1540 m/s and does not deviate significantly from this for most human soft tissues, but its estimation has been proposed to provide an indicator of tissue abnormality [**71**]. Published data for speed of sound data and measurement techniques are described by Bamber in reference [**11**]. In interesting recent work, Levy *et al.* [**72**, **73**] have proposed that a transmission-based (projection) imaging method be used to estimate the speed of sound dispersion (SOSD) as a means of breast cancer diagnosis, with other potential applications also suggested, including assessment of the heart and bone.
5. *Scatterer size*. The clinical hypothesis underpinning scatterer size estimation is that tissue microstructure (scatterer sources) of diseased tissue is different to that of healthy tissue. Early work by Lizzi *et al.* [**6**] on the eye, where attenuation effects are negligible, demonstrated the proof of principle that scatterer size can be estimated from the echo signal spectrum. Insana *et al.* [**74**] estimated the scatterer sizing from the cepstrum of the RF signal (Fourier transform of the logarithm of the power spectral density), assuming that the attenuation was known, as did Hall *et al.* [**75**]. In reference [**76**] it was shown that scatterer property estimation can be improved using prior knowledge about the expected SNR of the power spectrum, and in reference [**77**] the simultaneous estimation of attenuation and scatterer size from the backscattered power spectrum was investigated. Finally, Liu *et al.* [**78**] recently reported on using a capacitive micro-fabricated ultrasonic transducer (CMUT), offering a broader bandwidth than conventional piezoelectric transducers, for scatterer size estimation on a breast fibroadenoma.
6. *Nakagami parameter*. The Nakagami distribution provides a general model for the ultrasonic backscattered envelope under all scattering conditions and scatterer densities. The Nakagami distribution is defined as

$$f(r) = \frac{2m^m r^{2m-1}}{\Gamma(m)\Omega^m} \exp\left(-\frac{m}{\Omega} r^2\right) U(r)$$

where $\Gamma(\ )$ and $U(\ )$ are the gamma function and unit step function respectively. If R is the ultrasonic backscattered envelope and $E(\ )$ denotes the statistical mean, then the scaling parameter Ω and the Nakagami parameter m are defined as

$$\Omega = E\left(R^2\right)$$

and

$$m = \frac{\left[E\left(R^2\right)\right]^2}{E[R^2 - E(R^2)]^2}$$

where parameter m determines the shape of the distribution and is sometimes also called the shape parameter. As m varies between 0 and 1, the envelope statistics vary from a pre-Rayleigh to a Rayleigh distribution, and for $m > 1$ they have a post-Rayleigh distribution. Methods for estimating the Nakagami distribution and applying it to breast mass characterization are described in references [**18**] to [**20**].

Unfortunately, individual acoustic-based tissue parameters do not normally directly correlate with disease, which means that some sort of classifier has to be used to classify tissue based on multiple features derived from the RF signal or combined RF signal and B-mode image. There are many to choose

from in the literature [**79**]. Gefen *et al.* [**19**] used a linear and quadratic discriminant function, Chang *et al.* [**33**] used support vector machines, Scheipers *et al.* [**80**] used a fuzzy inference system, and Drukker *et al.* [**34**] used a Bayesian neural network. The classifier approach has proved particularly popular for tissue characterization problems such as the assessment of prostate cancer [**81**–**83**], parotid gland tumours [**80**], breast cancer [**19**], and renal disease [**84**].

Alternatively, the parametric images derived from the RF signal can be used instead of the B-mode intensity image within an image segmentation framework. This idea has been investigated, for instance, by Davignon *et al.* [**18**], who developed a multiparameter segmentation framework that was applied to phantom data. Dydenko *et al.* [**85**] and Yan *et al.* [**86**] have applied related ideas to the segmentation of 2D and 3D echocardiography images respectively. Basing image segmentation on tissue parameters derived from the RF signal is appealing from a theoretical point of view. However, in practice, the added computational cost of working with the large volume of RF data is at odds with the practical considerations that few ultrasound machines today offer RF signal access and that in many applications image segmentation needs to be very fast. As a consequence there are only a few publications using the RF signal for segmentation, although this number is likely to increase in coming years.

5 CONCLUSION

This article has presented a review of the ultrasound image segmentation and ultrasound tissue characterization literature. Both research fields are moving ultrasound towards becoming a more quantitative technique via both a better understanding of how to estimate acoustic properties in the presence of artefacts, and the design of more sophisticated image segmentation strategies that can handle uncertainty and make use of application-specific knowledge, including information derived from the RF signal.

This review has not discussed ultrasound image enhancement (preprocessing), including speckle reduction, which can improve the quality of ultrasound image segmentation. An interesting variant of ultrasound image enhancement that the author's group has been investigating is what has been called fusion echocardiography, in which ultrasound scans are aligned prior to image segmentation [**87**, **88**]. This leads to images with better anatomical definition, and which are easier to segment, at the expense of losing information about the physics of image formation.

Finally, this review has not touched upon some important areas of ultrasound tissue characterization that are described elsewhere in this Special Issue, including elastography [**89**], acoustic radiation force impulse imaging (ARFI) [**90**], and supersonic shear wave imaging [**91**]. Quantification of microbubble uptake using dynamic ultrasound imaging has also not been discussed (again, part of this Special Issue).

In conclusion, both ultrasound image segmentation and ultrasound tissue characterization are important areas of quantitative ultrasound research that are beginning to offer robust enough quantitative solutions for decision-making in clinical practice, and they are fields where technical advances are currently being made at a very fast pace.

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