A hybrid multi-scale model for thyroid nodule boundary detection on ultrasound images

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A hybrid model for thyroid nodule boundary detection on ultrasound images is introduced. The segmentation model combines the advantages of the “\textquotedblleft a trous\textquotedblright” wavelet transform to detect sharp gray-level variations and the efficiency of the Hough transform to discriminate the region of interest within an environment with excessive structural noise. The proposed method comprise three major steps: a wavelet edge detection procedure for speckle reduction and edge map estimation, based on local maxima representation. Subsequently, a multiscale structure model is utilised in order to acquire a contour representation by means of local maxima chaining with similar attributes to form significant structures. Finally, the Hough transform is employed with \textquoteleft a priori\textquoteright knowledge related to the nodule\textquotesingle s shape in order to distinguish the nodule\textquotesingle s contour from adjacent structures. The comparative study between our automatic method and manual delineations demonstrated that the boundaries extracted by the hybrid model are closely correlated with that of the physicians. The proposed hybrid method can be of value to thyroid nodules\textquotesingle shape-based classification and as an educational tool for inexperienced radiologists.

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1. \textbf{Introduction}

Thyroid nodules are very common findings located in the thyroid gland and may be indicative of thyroid cancer \cite{1}. They are diagnosed in approximately 2–7\% of the population in United States, Europe and Japan \cite{2–4}. When detected at an early stage, thyroid cancer is an extremely curable disease, thus an accurate differentiation between malignant and benign thyroid nodules is necessary to ensure proper clinical management of malignant nodules. The advent of high-resolution Ultrasound (US) technology as a preoperative diagnostic tool has made possible the acquisition of detailed information regarding the thyroid gland structure. Nowadays with contemporary US systems thyroid nodules can be located, measured and examined to determine whether a surgical intervention is needed or not. Besides echogenicity and presence of microcalcifications within the nodules \cite{5,6}, several other US characteristics such as nodule\textquotesingle s shape and contour can also be employed as malignancy risk factor criteria. An ill-defined margin or an irregular shape can be suggestive of malignancy whereas a round area indicates a benign lesion \cite{7,8}.

Despite its non-invasive nature, low cost and easy-to-use real time application, US imaging suffers from the presence of a granular pattern termed as speckle. It is the result of
various constructive and destructive interference phenomena, which occur when the distances between the tissue scatterers are smaller than the axial resolution limit of the system. It causes deformities of anatomic structures as well as random fluctuations in the image's intensity profile [9]. If an image is corrupted with speckle there are no regions of approximately constant intensity profile even if the reflecting tissue is entirely uniform. In addition, several US properties can lead to misleading effects in the ultrasound image. Reverberation, shadowing, refraction, side and grating lobes deteriorate the resolution of the US image, thus degrade its overall quality. The aforementioned problems arising by the complex nature of US imaging, constitute accurate boundary detection, a difficult task even for physicians with great expertise.

A correct boundary estimation of a thyroid nodule may play a key role in thyroid US imaging applications, such as classification in regard with the nodule’s shape, size and position. Furthermore, it may assist in the accurate needle placement during fine needle aspiration (FNA) biopsy procedure. Numerous computerized segmentation methods have been employed in US imaging of the prostate, kidney, cardiac anatomy, ovaries, fetal head and breast lesions. All these algorithms can be categorized in five types depending on the strategy chosen for segmenting the region of interest (ROI). Segmentation methods based on (a) edge detection [10,11], (b) texture or feature analysis [12–14], (c) deformable and active models [15,16], (d) methods based on combination of the above algorithms for optimization of the results [17–23] and (e) methods based on multiscale algorithms that visualise US images at different level of resolution [24–26].

An edge-based segmentation algorithm detects any abrupt changes in gray level values within the US image. For the final contour extraction an additional process is performed to select and link edge pixels. In texture analysis, rather than trying to locate edges in a US image, several texture features are employed for region characterization. These features usually serve as input to a classification or clustering algorithm to discriminate a group of pixels as correct or false regions. Model-based segmentation approaches use either a priori knowledge with named active contours and deformable models, or statistical models without the use of any prior information regarding the ROI. Multiscale methods decompose the input US image into several different levels of resolution in order to acquire all available information towards an efficient segmentation.

The poor US image quality in general, in conjunction with the drawbacks arising from the nature of ultrasound, limit the performance of various segmentation methods, proposed throughout the past decade. Most edge based techniques generally detect changes in the gray level profile and usually do not isolate and extract the ROI. Segmentation approaches based in textural characteristics are optimised for particular US images and suffer from the presence of adjacent tissues that exhibit similar acoustic properties. More complicated algorithms, based on active models or multi-scale analysis, are usually semi-automatic. In unsupervised algorithms the lack of detailed information regarding the way authors handle the presence of adjacent structures is worth noticing.

In the proposed method a multiscale hybrid model is introduced for unsupervised thyroid nodules boundary extraction from US images. Our approach, in order to overcome the texture limitations in US thyroid imaging, integrates a wavelet-based multiscale edge detection into an across scale structure detection model for a contour map estimation. The final contour map, derived from the introduced model, serves as input to a constrained Hough transform for nodule detection. The Hough transform is invariant to any open contours, which may be derived from the multiscale structure model.

At first, a speckle reduction-edge detection procedure is implemented based on a multi-fold wavelet-based analysis. A wavelet decomposition at four dyadic scales with the “á trous” algorithm is employed, in which speckle is removed via a coarse to fine analysis of wavelet transform modulus maxima (WTMM). The back-propagating local maxima with positive lipschitz exponents ‘a’ are considered of value and utilised in the subsequent multiscale structure model. On the other hand, back-propagating local maxima with negative lipschitz exponents are classified as speckle and discarded.

A multi-scale pixel representation is derived from the speckle removal-edge detection procedure, in which pixels of the input US image are associated with WTMM. A further step of this method is to consider a multi-scale structure representation, which would associate an anatomical object in the image with a volume in the multi-scale edge transform. A multi-scale structure model has been developed for boundary detection in US images. The principal components of the introduced model are the WTMM, the maxima chains which are groups of local maxima with similar properties at the same scale, the structures which are a set of connected maxima chains, the interscale relation which determines the criteria employed for the algorithm to relate maxima chains across scales into a significant structure and the structure operator that indicates in which structure a given maxima chain belongs to. All mentioned components are integrated to form a multi-scale contour representation. In order to extract the nodule’s boundary, the last scale of the contour decomposition is employed as input into the constrained Hough transform based in ‘a priori’ shape knowledge for partial circular object recognition. A schematic representation of the algorithm’s steps is depicted in Fig. 1.

The paper is organized as follows: in Section 2, the speckle reduction-edge detection proposed strategy is described. After that, a thorough analysis of the introduced multi-scale structure model is made, in which a structure map that corresponds to various image’s structures is acquired. Finally, the constrained Hough transform for detecting parameterized curves within the structure map, obtained from the previous step, is presented. In Section 3, the performance of the hybrid method applied on real US images is demonstrated through a comparative study between our method and the manually delineated nodules from two experienced physicians. Moreover, an inter-observer study was carried out between the two physicians to estimate the degree of variance the manually boundaries present. In the last section an extensive review and discussion regarding methodology, performance and potentials of the algorithm are given.
2.2. Edge detection procedure

2.2.1. Multiscale edge representation

Multiscale edge representation (MER) utilizes the local maxima of the dyadic wavelet transform (DWT) for characterization of signals from multi-scale edges. MER can be considered as a transformation from the initial US image representation into a feature representation based on the image’s intensity sharp variations defined as edges [27]. This transformation is considered as an intermediate step for analysis towards thyroid nodule segmentation. The proposed method decomposes the multiplicative speckle model into an additive signal dependent noise model, which in turn means that it omits the log-transform to avoid the mean bias correction problem [28,29].

The two-dimensional DWT is the set of functions \((W^1_{2j} f(x,y), W^2_{2j} f(x,y))\) and is given by:

\[
W^1_{2j} f(x,y) = \frac{1}{\sqrt{2}} \left( \psi^1_{2j} \ast f(x,y) \right)
\]

\[
W^2_{2j} f(x,y) = \frac{1}{\sqrt{2}} \left( \psi^2_{2j} \ast f(x,y) \right)
\]

where \(\psi^1(x,y)\) and \(\psi^2(x,y)\) are the analyzing wavelets, \(f(x,y)\) is a symmetrical smoothing function approximating the Gaussian, \(f\) is the image function \(f(x,y) \in L^2(\mathbb{R}^2)\) and \(j\) the dyadic scale.

Eq. (1) states that the dyadic wavelet transform at a given dyadic scaling factor, is the partial derivative of the convolution product between the US signal and a dilated smoothing function at that scale. The wavelet decomposition across scales of the original image was implemented with a filter bank algorithm, so called “algorithme à trous” (algorithm with holes) with Mallat’s filters. The Gaussian function is replaced by the cubic spline function producing the quadratic spline wavelets for the decomposition. The “à trous” expression denotes the insertion of \((2^j - 1)\) zeros in between the coefficients of the smoothing filters. These filters are “stretched” to take into account the rescaling while the convolution along the rows and columns is performed without any subsampling. This type of redundant wavelet transform is considered as shift-invariant which in turn makes it suitable for signal analysis, edge detection and segmentation purposes.

The two-dimensional wavelet transform of an image can be viewed as a gradient vector (Eq. (2)) whose magnitude and phase are given by Eqs. (3) and (4):

\[
\begin{align*}
W^1_{2j} f(x,y) &= 2^j \cdot \nabla f_0(x,y) \\
W^2_{2j} f(x,y) &= 2^j \cdot \nabla f_2(x,y)
\end{align*}
\]

\[
M_{2j} f(x,y) = \sqrt{W^1_{2j} f(x,y)^2 + W^2_{2j} f(x,y)^2}
\]

\[
A_{2j} f(x,y) = \tan^{-1} \left( \frac{W^2_{2j} f(x,y)}{W^1_{2j} f(x,y)} \right)
\]

The phase is quantized along eight possible directions \((0, \pi/4, \pi/2, 3\pi/4, \pi, 5\pi/4, 3\pi/2, 7\pi/4)\) corresponding to the eight neighbors of a pixel. At a given scale a point is considered as edge point if the magnitude of the gradient vector is locally maximum, compared with its two neighbors along

Fig. 1 – Schematic representation of the segmentation algorithm.

2. Materials and methods

2.1. US data acquisition

All US images used throughout this study were obtained from an HDI-3000 ATL digital ultrasound system – Philips Ultrasound P.O. Box 3003 Bothel, WA 98041-3003, USA – with a broadband (5–12 MHz frequency band) linear array. The sono-

graphic scans were taken in both the transverse and longitudinal plane and instrument settings were set accordingly to the built-in ‘SmallPartTest’ Philips protocol. The selected static US frames were digitized by a video card “frame grabber” (Miro PCTV, Pinnacle Systems) installed in a PC, capable of acquiring and displaying US images with a 768 × 576 resolution at 8 bits.

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the direction given by its quantized phase. For each local maximum its position, amplitude and angle are recorded.

2.2.2. Coarse to fine analysis

The next step afterwards MER is a coarse to fine procedure that employed all available information of WTMM at different frequency bands for pointwise singularity detection. Lipschitz regularity was the main criterion towards classification of edges as speckle or important sharp variations. The outcome of this procedure was a multi-scale edge map that relates all significant information of the US image with WTMM. The discrimination between edges that correspond to structures and those arising from speckle or artifacts was a two-folded process. At first, groups of maxima that back-propagate from coarse to fine scales were detected and formed vectors in the scale-space plane, and afterwards were utilized for singularity detection via the Lipschitz exponents $\alpha = [30]$. That inter-scale information is acquired by means of a back-propagation connectivity of the wavelet transform modulus maxima. The grouping of local maxima across scales is made on the basis that if an edge exists in a coarser scale, it can also be located in all available finer scales [31]. Two local maxima from two successive scales are grouped together if they possess a close position in the image plane and similar angle value. This back-propagation tracking, from the coarse to fine scale $2^j$ to the finer scale $2^{j-1}$, produces curves of maxima in the scale-space plane (termed as maxima lines, ML), which take the following form:

$$\text{ML}_k = \{ [M_{2j}, A_{2j}, P_{2j}], [M_{2j-1}, A_{2j-1}, P_{2j-1}], \ldots, [M_{21}, A_{21}, P_{21}] \} \quad (5)$$

where $M$, $A$ and $P$ are the magnitude, angle and position of each local maximum at a given scale $k$ and $n$ the total number of local maxima found in the coarsest scale $2^n$ where the back-propagation tracking is employed. The magnitude parameter is exploited in cases where a coarse local maximum is computed to back-propagate in more than one finer local maxima. In such cases the maximum with the greater magnitude is chosen to form the maxima line. The coarse to fine local maxima detection is made with a corresponding large to small investigation window, depending on the length of the dilated filter for each scale. In coarse scales the window is relatively the same with the corresponding dilated filter with $2^n - 1$ inserted zeros while in the finer scale available the window has the same size as the filter without dilatation.

The asymptotic decay from coarse to fine scales of the function’s wavelet transform along horizontal and vertical directions, given by $|W^1_f(2^j, x, y)|$ and $|W^2_f(2^j, x, y)|$ respectively, characterize the function’s Lipschitz regularity in the corresponding neighborhood. A function $f(x, y)$ is uniformly Lipschitz $\alpha$, $0 \leq \alpha \leq 1$ inside a bounded domain of $R^2$ if and only if there exists a constant $K > 0$ such that for all $(x, y)$ inside this domain and for any dyadic scale $2^j$:

$$|M_f(2^j, x, y)| \leq K(2^j)^{\alpha} \quad (6)$$

The decay of $\log_2 |M_f(2^j, x, y)|$ as a function of $\log_2 j$ is estimated along all maxima lines that correspond to singularities with varying Lipschitz regularity. When the maxima amplitude within the maxima line decreases when the scale decreases its Lipschitz regularity is positive (positive Lipschitz exponents). On the contrary, in a maxima line with maxima amplitudes that increase when the scale decreases the Lipschitz regularity is negative (negative Lipschitz exponents). The local maxima being part of maxima lines with positive Lipschitz exponents correspond to important edges, whereas local maxima inside maxima lines with negative Lipschitz exponents correspond to speckle. After the coarse to fine analysis the back-propagating maxima with positive Lipschitz regularity are utilized as input to the subsequent multi-scale structure model. A pseudo code of the coarse to fine analysis that constructs a speckle free multiscale edge map is depicted below.

**Pseudo Code 1**

```plaintext
function COARSE TO FINE ANALYSIS returns speckle-free multiscale edge map
inputs: \( N \) = 4, the maximum decomposition scale.
\[ M_{2^j} f(x, y) \leq j \leq N \], Local maxima position and amplitude across decomposition scales.
\[ A_{2^j} f(x, y) \leq j \leq N \], Local maxima phase values across decomposition scales.
for each \( M_{2^j} f(x, y) \) do
    for all finer scales: \( 2^j \leftarrow 2^i \) do
        find \( M_{2^j} f(x, y), M_{2^i} f(x, y), M_{2^j} f(x, y) \) with similar position and phase values.
        construct maxima line vector: \( \text{ML} \leftarrow [M_{2^j} f(x, y), A_{2^j} f(x, y)] \) \( 1 \leq j \leq 4 \)
        calculate decay slope of \( \log_2 \text{ML} \leftarrow \log_2(M_{2^j} f(x, y), 1 \leq j \leq 4) \)
        if decay slope is positive then return \( \text{ML} \leftarrow [M_{2^j} f(x, y), A_{2^j} f(x, y)] \) as important edge across scales
        else if decay slope is negative then return \( \text{ML} \leftarrow [M_{2^j} f(x, y), A_{2^j} f(x, y)] \) as speckle and discard it
```

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The implementation of the MER requires the computation of the wavelet transform for scales $2^1$ to $2^N$. The choice of the parameter $N$ depends on the application. For feature extraction and segmentation methods the choice of $N$ is crucial. The Lipschitz regularity calculation of two adjacent singularities, considered as prerequisite that the two sharp variations are isolated. As the dilation of the wavelets and the smoothing function are increased, the resulting singularities will begin to overlap. In order to estimate the optimum dyadic level, the location of each sharp variation is associated with the WTMM. In this study, it is experimentally shown that the localization of WTMM is increased from $N = 1$ to 4. From this scale and on, the evolution of WTMM across scales produce localization and numerical errors. In fact, the majority of local maxima tracked at scale $N = 4$ are converted into a single maxima at $N = 5$ whereas a small fraction demonstrates irregular behavior, which in turn produces negative Lipschitz exponents between these two scales.

2.3. Multi-scale structure model

The proposed structure model considers a significant structure as a hierarchical set of connected maxima chains. A structure representation is obtained, in which structures are bridged maxima chains with similar properties across all available scales. The fundamental parameters that the introduced model employs to generate the multi-scale structure representation, are presented below:

- Local maxima: the back-propagating WTMM derived from the speckle reduction-edge detection step.
- Maxima chains: WTMM are grouped together in each available scale with similar properties forming one-dimensional curves, termed as maxima chains. A chain ($C$) is a set of linked local maxima at a given scale $2^j$:

$$C_{2^j} = \{ [M_{2^j}f(x_1, y_1)], [M_{2^j}f(x_2, y_2)], \ldots, [M_{2^j}f(x_p, y_p)] \}$$

(7)

where $M$ is the amplitude, $k$ and $p$ the number of chains and local maxima included in the chain respectively.
- Structures: a structure is a set of connected maxima chains at the same scale. A significant structure derived from adjacent chains is of the form:

$$S_{2^j} = \{ [C_{2^j, 1}], [C_{2^j, 2}], \ldots, [C_{2^j, i}] \}$$

(8)

where $i$ is the number of adjacent maxima chains bridged to form a structure and $2^i$ the coarsest scale.
- Inter-scale relation: the criteria employed for the algorithm to relate maxima chains across scales into a single structure.
- Structure operator: which indicates to which structure a given maxima chain belongs to.

2.3.1. Maxima linking

The previous edge detection procedure generated a speckle-free multi-scale pixel representation, where each pixel corresponds to WTMM emanating from various structures located within the US image. Nevertheless, individual wavelet maxima are mostly not independent features; they are part of certain lines or curves localized in multiple scales. The initialization of the model is implemented as global searching of WTMM in each scale with matching properties. The maxima chain linking procedure creates curves comprising of local maxima groups at each scale. The connectivity procedure is a complicated operation dependent on directional compatibility, spatial adjacency and amplitude similarity. The latter can be rephrased as two edge-points in a given scale, linked to form a maxima chain on condition that they are close to each other and have similar phase and amplitude values.

2.3.2. Structure identification

Despite the chaining procedure, small gaps between adjacent maxima chains are created resulting to a broken outline. The main reasons of this inadequacy are: probable transducer displacement from the physician during US examination, various acoustic phenomena such as refraction, shadowing and reverberation, and numerical errors made during the calculation of the coarse to fine evolution of WTMM. These numerical errors are caused by the fact that the wavelets used (quadratic spline) are not the derivative of a Gaussian but only an approximation. An efficient structure representation prerequisites continuity of chains.

The rule applied to connect two maxima chains into a single structure is termed as ‘inter-scale relation’. All maxima chains located in the multi-scale edge map correspond to significant segments of a broken borderline. Each of the maxima chains is approximated by its mean and position. This approximation of a maxima chain is expressed by the following equation:

$$C_{2^j} = \left\{ \left( \left( \sum_{p=1}^{P} \frac{M_{2^j, 1}, M_{2^j, 2}, \ldots, M_{2^j, P}}{P} \right) \right), \left[ P_{2^j, 1}, P_{2^j, P} \right] \right\}$$

(9)

where $2^j$ is the dyadic scale, $M_{2^j, p}$ are the amplitude values of the chain, $p$ the number of local maxima and $P_{2^j, 1}, P_{2^j, P}$ are the chain’s maxima starting and ending positions. Two maxima chains at two successive scales $C_{2^j} - C_{2^{j+1}}$ are said to belong to a single structure because of their maxima positions proximity. This means that the majority of the local maxima compose a maxima chain $C_{2^j}$, must also be contained in the maxima chain $C_{2^{j+1}}$. Moreover, two adjacent maxima chains at a given scale comprise a single structure due to position and mean-amplitude similarity.

All maxima chains, appearing in successive scales that satisfy the above two rules are connected in such a way to form a structure. In each structure defined as a set of maxima chains, an operator $L$ is assigned which indicates the arithmetic label given at each detected group of connected maxima chains: $L(C_{2^j, i}) = i$, where $i$ is the number of maxima chains and $i$ the arithmetic label of each structure. In the resultant structure representation any individual maximum that is not linked during the chaining is removed. A pseudo code of the structure detection procedure that constructs the multiscale structure.
Once the structure representation has been implemented
the structure image from the coarsest scale is transformed
into a boolean one (i.e. pixel intensity equals 1 when a max-
mum is detected and zero otherwise). An additional step is
required to separate and detect the important structure that
coincides with the thyroid nodule from other various struc-
tures that correspond to different anatomical regions located
in the US image.

2.4. Nodule’s boundary extraction

The boundaries of several anatomical parts investigated in
medical imaging such as kidney, prostate, parts of the heart
and of course thyroid nodules can be approximated by reg-
ular curves. As already stated in the introduction section,
despite the irregularity degree of its contour, every thyroid
nodule retains a partial circular shape [5–8]. The edge detec-
tion methods do not extract the ROI. In optimal algorithm
performance, the candidate anatomical structure is revealed
noise-free in the xy-plane surrounded by other anatomical
structures present in the medical image. An efficient tech-
nique to isolate features of a particular shape within an
image is the Hough transform. The classical Hough trans-
form can be employed in applications where a simple analytic
description of a feature is not possible [33]. Due to the compu-
tational complexity of the generalized Hough algorithm, we
have restricted our boundary extraction attempt within the
framework of the classical Hough transform.

2.4.1. Constrained Hough transform

The main idea of the Hough transform can be considered as
a point to curve transformation from a Cartesian image space
map in the Hough parameter space. When viewed in Hough
parameter space, points that are collinear in the Cartesian
image space become readily apparent as they yield curves,
which intersect at a common point. From the synthetic image
of Fig. 2(a), a boolean map is derived with labeled structures
representing different anatomical regions located in
the US image.

Once the structure representation has been implemented
the structure image from the coarsest scale is transformed
into a boolean one (i.e. pixel intensity equals 1 when a max-
mum is detected and zero otherwise). An additional step is
required to separate and detect the important structure that
corresponds to the thyroid nodule from other various struc-
tures that correspond to different anatomical regions located
in the US image.

function STRUCTURE DETECTION returns multiscale structure representation
  // maxima chain construction
  inputs: N = 4, the maximum decomposition scale.
  Multi-scale Edge Map with \[ M_{j}^{f(x,y)} \] \( \leq j \leq 4 \) \( \rightarrow \) local maxima classified as important edges
  for each scale: \( 2^{j} \) \( \leq j \leq N \) do
    find \( M_{j}^{f(x,y)} \) with similar position, amplitude and phase values.
    construct maxima chain: \( C_{j}^{M_{j}^{f(x,y)}} \)
  // structure detection
  for each \( C_{j}^{2^{j}} \) do
    for all finer scales: \( 2^{j} \rightarrow 2^{i} \) do
      if there are maxima chains \( C_{3}^{3}, C_{2}^{2}, C_{2}^{1} \) with similar position values
        construct unified maxima chain across scales: \( C_{j}^{M_{j}^{f(x,y)}} \)
      and if two adjacent maxima chains \( C_{j}^{i}, C_{j}^{i+1}, \ldots, C_{j}^{j} \) \( \leq j \leq 1 \) with position and amplitude proximity
      assign structure operator: \( L \rightarrow L(C_{j}^{i}, \ldots, C_{j}^{j}) \)
      construct structure \( S_{j}^{i} \)

PSEUDO CODE 2

\( \sum_{j=1}^{p} r_{i}^{2} = (x_{i} - x_{ref})^{2} + (y_{i} - y_{ref})^{2} \) (10)
where \( x_{i}, y_{i} \) are the coordinates and \( p \) the number of the con-
nected maxima for each structure.
Circles are projected around the candidate center-point, and for each maxima point on the structure boundary, the corresponding cell in the accumulator array is incremented by one. The accumulator matrix representing the Hough parameter space has the same dimensions as the original, and the method involves projecting circles using Cartesian coordinates (Fig. 2(b)).

2.4.2. Accumulator local maxima detection
As a result in the parameter space those reference points located within circular objects (i.e. thyroid nodule) are related with relatively large values in the accumulator array, in contrast to other structures (i.e. veins, arteries, etc.). In Fig. 2(c) we can observe that the cell approximately corresponding to the simulated nodule’s center appears as the maximum value in the parameter space. A local maxima detection procedure is applied in the accumulator array to find the approximate center. Subsequently, its corresponding structure is superimposed on the image as the final segmentation outcome (Fig. 2(d)).

2.5. Algorithm implementation
The software development of the proposed method and the user-friendly software for manual delineation from the two observers was implemented with Matlab 6.5. The computer used for processing has an AMD Athlon XP+ processor running at 1.8 GHz and 512 of RAM.

3. Results
The overall segmentation procedure (edge detection – multi-scale structure representation – nodule’s boundary extraction) employed towards an efficient boundary detection in two US images with an isoechoic and a hypoechoic thyroid nodule, is depicted in Figs. 3 and 4, respectively.

To evaluate the performance of the proposed segmentation method, a comparative study was employed, comprised 40 US thyroid images from 40 female patients between 40 and 65 years old. All images were randomly chosen from a greater US image database collection acquired from an experienced radiologist (N.D.). The proposed method’s segmentation results were compared with the delineated boundaries (used as ground truth) drawn from two experienced observers (OB₁ and OB₂) in terms of nodule area, roundness, concavity and mean absolute distance (MAD).

The area of each nodule is calculated by measuring the pixels inside the nodule’s borders. Roundness characterizes the circularity of the nodule and takes low values for circular nodule and high for irregular boundaries [34]. The nodule's...
Fig. 3 – (a) US image with an iso-echoic thyroid nodule, (b) contour representation, (c) constrained Hough transform, (d) accumulator array, (e) outcome of the hybrid model, and (f) manually delineated boundary.

roundness is defined as:

\[
\text{roundness} = \frac{\text{perimeter}^2}{\text{area}} \tag{11}
\]

The perimeter is measured by summing the number of pixels on the border of the nodule. Concavity is a shape feature that indicates the presence of concave regions [34]. It is measured by dividing the mean value of the Euclidean distances between the centroid and the convex hull (CV) pixels with the mean value of the Euclidean distances between the centroid and the actual boundary (AB) pixels:

\[
\text{concavity} = \frac{\frac{1}{M} \sum_{i=1}^{M} \sqrt{(Y_{\text{centroid}} - Y_{\text{CV}})^2 + (X_{\text{centroid}} - X_{\text{CV}})^2}}{\frac{1}{N} \sum_{i=1}^{N} \sqrt{(Y_{\text{centroid}} - Y_{\text{AB}})^2 + (X_{\text{centroid}} - X_{\text{AB}})^2}} \tag{12}
\]

The MAD characterizes the shape difference evaluation between two contours [21]. If two given curves are represented as point sets: \( A = \{a_1, a_2, \ldots, a_m\} \) and \( B = \{b_1, b_2, \ldots, b_m\} \) the
Fig. 4 – (a) US image with a hypo-echoic thyroid nodule, (b) contour representation, (c) constrained Hough transform, (d) accumulator array, (e) outcome of the hybrid model, and (f) manually delineated boundary.

Regarding the MAD parameter, in order for the results to be numerically comparable with the other three parameters, the percentage MAD% parameter is introduced. It is considered as the percentage pixel area difference between the automatic and manual boundaries. The distances summation of each pair automatic (AU)-manual boundary (OB) is subtracted from the total number of pixels within each manual boundary (OB). The result of this operation is converted in terms of percentage. High MAD% values suggest that the great majority of pixels within the manual boundary area (used as ground
The actual MAD values, calculated as the average of the distances, were 2.54 for the set of pairs AU-OB1 and 2.16 for the set of pairs AU-OB2 with standard deviations 0.88 and 0.83, respectively. — Table 2.

### 3.1.1. Inter-observer variability

US regular diagnostic procedure is highly subjective, thus ideal boundaries for the thyroid nodules are difficult to acquire. In order to assess any potential variation in boundary recognition, an inter-observer study was also performed for the two observers. The actual MAD values, calculated as the average of the distances, were 2.54 for the set of pairs AU-OB1 and 2.16 for the set of pairs AU-OB2 with standard deviations 0.88 and 0.83, respectively — Table 2.

#### Table 2 – Mean values and standard deviation of the computed MADs for the pairs AU-OB1 and AU-OB2

<table>
<thead>
<tr>
<th>MAD (pixels)</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Automatic-observer 1 (AU-OB1)</td>
<td>2.54</td>
</tr>
<tr>
<td>Automatic-observer 2 (AU-OB2)</td>
<td>2.16</td>
</tr>
</tbody>
</table>
expert radiologists specialized in ultrasonography. The manual delineation in this study for all US images was done independently. Inter-observer agreement was determined using the weighted K (kappa) coefficient [35] calculated for all parameters employed in the previous comparative study. The ideal boundary was selected as the vector space union of each manual borderline pair. The threshold chosen for each parameter, in order for a manual boundary to coincide with the ideal one, was set to 90% agreement. A kappa statistic above 0.75 is taken arbitrarily to show excellent agreement, between 0.40 and 0.75 as substantial agreement and below 0.40 as poor agreement—Table 3.

The comparison of the two manually segmented nodules regarding area, roundness, concavity and MAD gave agreement rates on average approximately 90.77, 91.39, 92.25 and 92.91%, respectively with an overall percentage agreement of 91.83%.

### 4. Discussion

A new segmentation technique for automatic boundary extraction of thyroid nodules in US imaging is designed. The contribution of this approach is the integration of wavelet-based coarse to fine singularity detection, multiscale structure model, and the constrained Hough transform. In the comparative study, thyroid nodule segmentation accuracy reached approximately 90.14 and 89.33% in respect with the two observers. The percentage agreements between the derived and the manually delineated boundaries are within the interobserver range (91.83%). The MAD values, between the derived and the manual delineated boundaries (2.16–2.54), also coincide with the values other studies have presented [1.37–4.55] [21–23]. The inter-observer study demonstrated high kappa coefficient agreement of approximately 0.83. Although the algorithm is unsupervised, the evaluation results may be regarded as most encouraging considering the reduced US image quality. The proposed algorithm may be of value for computer-assisted systems aiming to support the standard diagnostic procedure as an objective second opinion tool.

The local maxima representation employed to construct the speckle-free-multiscale edge map not only does it identify edges but also characterizes them. The integration of local maxima via a coarse to fine method led to the different classification of edges based on their regularity. As a result, strong edges arising from significant structures are utilized in the subsequent structure model, whereas edges corresponding to speckle were discarded. Regarding the maxima chaining procedure, similar maxima linking attempts [31,36] have adopted a thresholding procedure based on the number of adjacent local maxima only in the last scale available to isolate the ROI.

The complex nature of US imaging often provides maxima chains with relatively small number of linked local maxima (two or three contiguous maxima) that might be a part of a greater structure contour. In contrast to these studies, the proposed multiscale structure model utilizes all local maxima existing in the edge map across scales, in order to reconstruct the best possible contour map.

Besides the presence of speckle, another major difficulty that all segmentation approaches encounter, is the existence of various anatomical structures located within the image. In very noisy structural environments, ROI isolation is an extremely difficult task. Most proposed methods also attempt to calculate a closed contour as a final segmentation outcome. The constrained Hough transform employed in this study, not only is it relatively unaffected by structure noise, but manages to isolate all thyroid nodules despite the fact that sometimes the nodule contour is not closed. In cases of diffusion between the nodule and the surrounding tissue, the algorithm does not guess the nodule boundary in that region, thus leaves this important clinical information for the physician. In addition, due to the fact that nodules are not perfect circles, the radius of the contour is variable and the accumulator array local maxima detection is made in a small area rather than in a single point.

The different echogenicity behavior of thyroid nodules (hypo-, iso- or hyper-echoic) limits the accuracy of thyroid nodules segmentation algorithms based on texture characteristics [37]. The edge-based technique presented in this article is echogenicity invariant as we can observe in Figs. 3 and 4, in which an iso-echoic and a hypo-echoic nodule are successfully segmented. Apparently, the hybrid algorithm can be employed to segment various anatomical structures viewed via US imaging with only one constrain: the ‘a-priori’ shape knowledge selection regarding the structure of interest.

The outcome of the edge detection stage is highly dependent on the radiologist’s competency in performing the US examination. Any possible misplacement of the transducer or the occurrence of various acoustic phenomena such as reverberation or shadowing, may produce a false contour map. The proposed algorithm identifies sharp variations with great accuracy wherever they occur but do not approximate the edges that are not visible in the image. In US images, where the thyroid nodule is partially visible or greatly distorted due to aforementioned acoustic phenomena, the proposed algorithm faced problems during the edge detection procedure. All the cases that had these drawbacks were omitted from the comparative study.

The incorporation of the generalized form of the Hough transform for arbitrary shape detection into the maxima chaining procedure across scales, may avoid most of the problems encountered by the majority of edge detection approaches. Nevertheless, the fine-tuning between the interscale wavelet maxima chaining and Hough transform algorithms, along with the extensive compilation time of the Hough transform are main drawbacks towards this segmentation approach.

The aforesaid potential problems of any segmentation approach necessitate the continuous investigation for an optimal segmentation technique. A parallel wavelet-based study is under research and development from the same team, based...
5. Conclusion

As a conclusion, a new efficient segmentation technique for thyroid nodule segmentation in sonography is introduced with promising results. The proposed algorithm is able to outline with high accuracy thyroid nodules regardless their texture, possible discontinuities in the boundary line and the presence of extensive structure noise. The method was evaluated in comparison with two experienced observers and demonstrated great agreement accuracy. The utilization of the hybrid method may assist a shape-based thyroid nodule categorization from the physician. Also, it might enhance the accuracy of the fine needle aspiration procedure thus offer several advantages in the decision-making procedure. Moreover, it can be used as an educational tool for inexperienced radiologists.

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