COMPUTER-BASED NODULE MALIGNANCY RISK ASSESSMENT IN THYROID ULTRASOUND IMAGES

Ioannis Legakis,* Michalis A. Savelonas,** Dimitris Maroulis,** and Dimitris K. Iakovidis**

Abstract

This paper presents a computer-based approach for detection, delineation, and malignancy risk assessment of thyroid nodules in ultrasound (US) images. The proposed approach is automatic and integrates processes for: the thyroid gland boundaries detection, the detection of nodular lesions within the thyroid gland, the delineation of the detected nodules, and the classification of thyroid nodules according to malignancy risk. These processes embed textural and shape feature vectors derived from the US images, as well as state-of-the-art medical image analysis and pattern recognition tools. The obtained classification performance, which is associated with automatic malignancy risk assessment, was evaluated by means of the receiver operating characteristic (ROC), demonstrating an area under curve (AUC) equal to 0.93. The quantification of the results shows that the proposed approach: (1) contributes to the objectification of the diagnostic process by the utilization of explicit image features, whereas it can provide the diagnosticians with a second opinion, (2) is applicable in clinical practice and could contribute to the reduction of false medical decisions.

Key Words

Thyroid nodules, ultrasound, computer-based medical approaches, malignancy risk assessment

1. Introduction

Thyroid nodules are solid or cystic lumps within the thyroid gland, involving occurrences of papillary, follicular, medullary and anaplastic carcinomas, with a considerable clinical importance. The prevalence of thyroid nodules increases with age, extending to more than 50% of the world's population, whereas 50% of people with solitary nodules detected by experienced physicians have additional nodules detected when further examined by ultrasonography. Approximately 5% of all nodules are found to be malignant, as proved by fine needle aspiration (FNA) biopsy examinations [1].

Ultrasound (US) is the most widely employed technique for thyroid gland screening, since it combines low cost, short acquisition time, absence of ionizing radiations and sensitivity in ascertaining the size and number of nodules. Moreover, it provides information on their structure and characteristics. However, US images contain echo perturbations and speckle noise, which could impede the diagnostic task. Additionally, the interpretation of these images is subjective, as it has been associated with high inter-observer variability [2, 3].

Echogenicity, texture and shape of thyroid nodules are features that have been demonstrated to correlate with nodule pathology [3, 4]. Tomimori *et al.* [5] proposed an US classification of thyroid nodules into four grades with increasing score numbers (1–4), associated with malignancy risk. Example cases of these four grades are illustrated in Fig. 1. Major malignancy indicators addressed by this classification include low echogenicity, and irregular or ill-defined boundaries. A precise US image delineation method capable of capturing these features or indicating their presence to the experts could contribute to the objectification of medical decisions, and could also be used as an educational tool for trainee radiologists.

Most of the previous works on US image segmentation are intensity-driven, as it is the case with the segmentation model proposed in [6] for the delineation of nodules on thyroid US images. This model copes with the presence of intensity inhomogeneity in thyroid US images, considering information from sparse background regions. However, its application is limited to hypoechoic or hyperechoic nodules, whereas the malignancy risk of isoechoic nodules, is considerable as well [3].

Another recent work on thyroid nodule delineation in US images is the hybrid multi-scale method [7], which involves a wavelet-based edge detection method and Hough transformation of the US images for the delineation of thyroid nodules regardless of their echogenicity. However, this method involves the classic instance of the Hough transform for circles detection which considers a-priori circular shapes for the nodules, thus limiting its practicality.

* Henry Dunant Hospital, Mesogion 107, 11526, Athens, Greece; e-mail: ilegak@med.uoa.gr

** Department of Informatics and Telecommunications, University of Athens, 15784, Athens, Greece; e-mail: {msavel, dmaroulis, diakov}@di.uoa.gr

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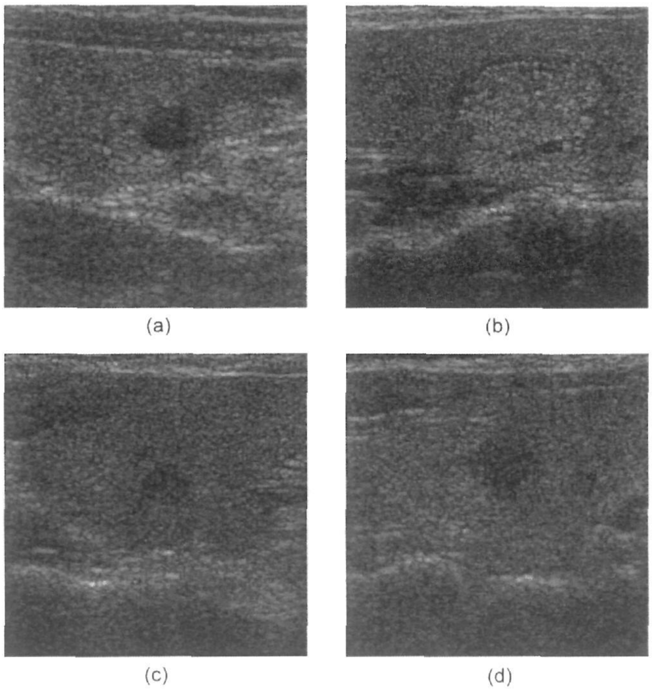


Figure 1. Thyroid US images containing nodules associated with: (a) grade I, (b) grade II, (c) grade III, and (d) grade IV, according to the US grading proposed by Tomimori *et al.* [5].

Moreover, the edge detection procedure used makes the whole process sensitive to the presence of US noise.

Recent attempts on categorization of thyroid nodules in US images include the utilization of intensity features extracted by the application of Radon transformation [8], as well as classification based on textural features extracted from gray level spatial-dependence matrices [9, 10].

In the present study, we validate thyroid US images from the outpatient's endocrinology clinic records in Henry Dunant Hospital, using an integrated computer-based approach for nodule boundary detection and malignancy risk assessment. It should be noted that such an integrated approach for computer-aided diagnosis of thyroid nodules in US images has not been proposed in the literature.

2. Materials and Methods

In this study, we retrospectively reviewed the records of 142 patients in a consecutive series, without prior thyroid surgery or radioiodine exposure, that were referred to the endocrinology unit in Henry Dunant Hospital between November 2004 and March 2007 for evaluation of suspected thyroid nodular disease. Female patients examined were 83 with mean age 43 ± 17, whereas male patients were 59 with mean age 56 ± 13. The criteria for referral were suspicion of the presence of one or more thyroid nodules by physical exam or the presence of an "incidental" nodule discovered by an imaging technique such as magnetic resonance imaging, computed tomography, or carotid ultrasound.

For each nodule, sonographic images were reviewed from three expert radiologists participating in this study, and sonographic characteristics were recorded. For eac nodule, the following sonographic characteristics wer recorded: size, parenchymal composition, echogenicity, an margin appearance. Size was recorded as three orthogon dimensions.

The US images were acquired using a digital US imag ing system Phillips HDI 5000 with a 12-MHz linear tran ducer in the radiology department of Henry Dunant Ho pital in Athens, Greece.

A special purpose software suite in Microsoft Visu C++ was developed and executed on a 3.2-GHz Intel Pe tium IV workstation, implementing the TBD algorithm as well as the algorithms for the localization of thyroi nodules, the delineation of thyroid nodules, and the fe ture extraction and classification. A total of 142 longit dinal *in vivo* digital images of thyroid nodule cases we acquired at a resolution of 256×256 pixels with a 25 grey-level depth. Dynamic range was set to 150 dB/C whereas thermical and mechanical indexes were set to 0. and 0.46, respectively. Three expert radiologists provide the "ground truth" thyroid gland boundaries, the locatio of nodular lesions, manual delineations of thyroid no ules, and classification of thyroid nodules according to th grading introduced by Tomimori *et al.* (Fig. 1) [5].

The proposed computer-based approach (JET) is a tomatic and comprises of four main processes: (1) th boundaries of thyroid gland are detected, (2) nodular l sions are detected and localized within the thyroid glan with the utilization of textural features, (3) an image se mentation approach based on active contours is applied f the accurate delineation of thyroid nodules, (4) a suppo vector machine (SVM), utilizing echogenicity, texture an shape features, is applied on each US image region, whic has been marked as nodular, so as to allow the classificatio of each nodule according to malignancy risk.

2.1 Detection of Thyroid Gland Boundaries

The lobes of thyroid gland are surrounded by a thin fibro capsule of connective tissue [11]. That capsule bound the thyroid gland and can be identifiable in longitudin US images as thin hyperechoic lines. The first phase the proposed thyroid US image analysis scheme aims t the detection of those lines. Detection is performed by thyroid boundaries detection (TBD) algorithm, propose by Keramidas *et al.* [12]. This algorithm involves thr stages: (a) pre-processing of the US image, (b) analys of the pre-processed image, and (c) identification of th thyroid boundaries.

The first stage involves normalization and unifor quantization of the original thyroid US image (Fig. 2(a into z discrete grey levels. Grey level quantization resul in a rough segmentation of the US image and accentuat the hyperechoic bounds of the thyroid gland (Fig. 2(b)).

In the second stage of the TBD algorithm, the qua tized image is vertically sampled from top to bottom wi horizontal stripes (Fig. 2(c)). An index associated with th number of pixels of each grey level is calculated for ea stripe. The rate of change of each grey level index betwe two successive stripes is estimated.

In the final stage of the TBD algorithm, the stripes that contain the outer and the inner thyroid boundaries are selected (Fig. 2(d)). Both boundaries should satisfy conditions involving the rates of change of grey level indexes, as well as an additional limitation, which imposes a minimum anteroposterior diameter of the thyroid gland.

2.2 Detection and Localization of Nodular Lesions

The boundaries detected by the TBD algorithm when applied on a thyroid US image (Fig. 3(a)) define a region of interest (ROI) (Fig. 3(b)) that usually contains a nodule or a cyst, in which feature extraction and classification take place. This ROI is raster scanned with sliding windows (Fig. 3(c)), and from each window a textural feature vector is extracted. The feature extraction method used for texture analysis of the thyroid gland is based on local binary patterns (LBP) [13], a texture descriptor well-known in image analysis community, which assigns a unique code to each local intensity pattern. This texture descriptor was chosen since it is highly discriminative, it involves low complexity computations, and it has been successfully applied for US image analysis [14].

Feature extraction is succeeded by classification of the feature vectors into two classes: a class of normal tissue regions and a class of nodular tissue regions. A simple k-nearest neighbour (k-NN) algorithm was selected as a powerful and robust non-parametric classification method with well-established theoretical properties that has demonstrated experimental success in many pattern recognition tasks [15].

It should be noted that within the context of the proposed computer-based system, nodular lesion detection and localization serves as an efficient process for the initialization of the subsequently applied image segmentation approach.

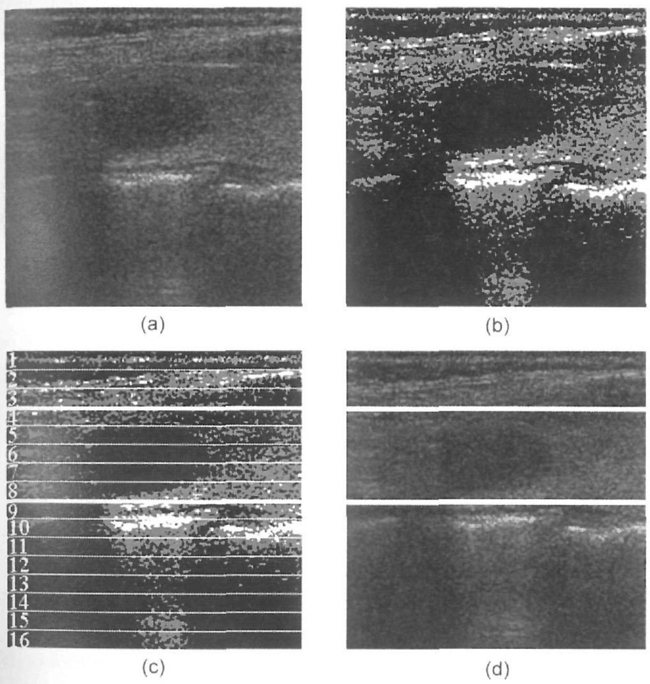


Figure 2. (a) Input thyroid US image digitized at 256 grey levels, (b) pre-processed US image quantized at 3 grey levels, (c) horizontal stripes sampled from the pre-processed image for analysis, and (d) the detected thyroid boundaries superimposed to the original input image.

2.3 Delineation of Thyroid Nodules

An image segmentation approach based on active contours [16] is employed to obtain accurate delineations of thyroid nodules. Active contours are self-adapting state-of-the-art image segmentation approaches. They can be relatively insensitive to noise by involving integral operators, which provide an inherent noise filtering mechanism [17], a feature of particular importance in the case of US images. Moreover, they can be formulated so as to offer the ability to delineate multiple nodules, as well as to cope with the presence of intensity inhomogeneity related to thyroid tissue and microcalcifications. Details on the mathematical formulation of the utilized texture-driven active contour can be found in [18].

Figure 4 illustrates an example delineation obtained by the utilized active contour (Fig. 4(b)), as opposed to the manual delineation obtained by an expert radiologist (Fig. 4(a)).

2.4 Malignancy Risk Assessment

In the last stage of the proposed computer-based approach, the nodular regions delineated by the active contour, are

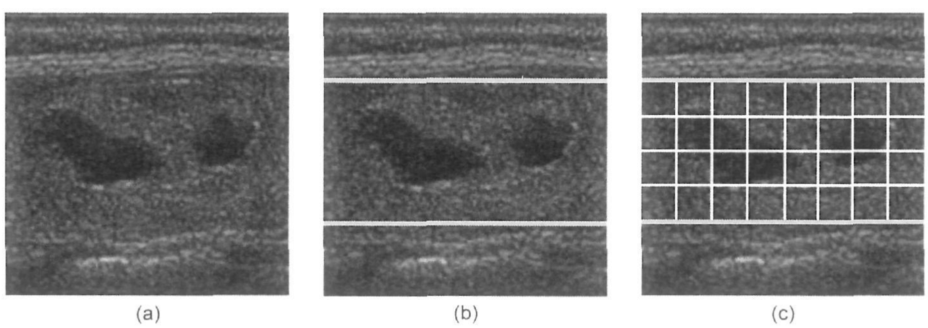


Figure 3. (a) Longitudinal US image of a thyroid gland, (b) ROI defined by the TBD algorithm, and (c) raster scanned ROI with sliding windows for feature extraction and classification.

classified according to their risk for malignancy. The classification is based on textural and shape features.

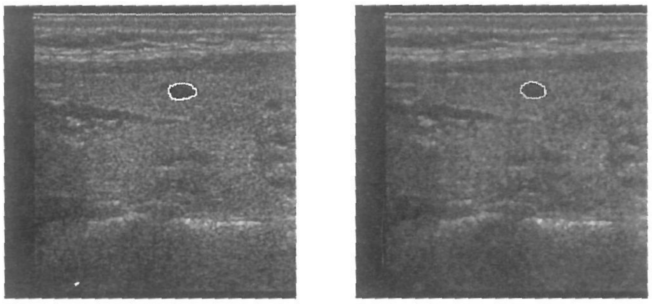
Radon domain [19] features have been considered for textural information encoding. The shape information is encoded by means of chain code (CC) histogram [20], compactness (CMP) [21], and fractal dimension (FD) [14]. Typically, benign masses are expected to have lower values of CMP as compared to malignant tumors [22]. FD indicates the presence of self-similarity at several levels of magnification and constitutes another measure of boundary irregularity. Microlobulated or highly spiculated contours of malignant tumors are expected to demonstrate fractal behaviour, which should be absent in the case of benign masses [23,34].

An SVM classifier [25] was used for the classification. In accordance with the recommendation in [26], 10-fold cross validation was performed for the generation of ROC curves.

3. Results

3.1 Detection of Thyroid Gland Boundaries

Experiments were performed to determine the optimal stripe dimensions that minimize the error between the boundaries detected by the TBD algorithm and the ground truth boundaries. In all the experiments a total of Three quantization levels was found to be sufficient. The optimal stripe dimensions lead to a mean accuracy in the detection of thyroid boundaries, which reaches $93.2 \pm 3.2\%$. For large values of stripe height, a notable decrement of the accuracy is observed as the large stripe size leads to a gross localization of the thyroid boundaries.



(a) (b)

Figure 4. Example run of the active contour model: (a) manual delineation and (b) delineation obtained with the active contour.

3.2 Detection and Localization of Nodular Lesions

Experiments were performed to evaluate the performance of the proposed scheme with the TBD algorithm in comparison with the conventional, exhaustive feature extraction scheme. The proposed scheme was tested for various window sizes, sliding steps, LBP neighbourhoods, and k-NN classifiers.

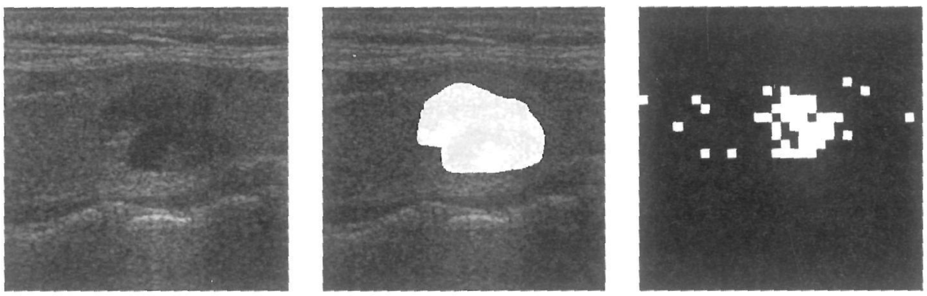
A balanced proportion of normal and abnormal samples was extracted from the available US images, ensuring that all samples corresponding to nodular thyroid tissues were included. According to pattern recognition theory [27], such a balanced dataset is expected to enhance the classification of abnormal samples and thus increase the system's sensitivity.

The classification accuracy obtained was 82.3% by previously applying the TBD algorithm, whereas it was 73.8% without previously applying the TBD algorithm. However, this accuracy cannot be accounted as a measure of the performance of the proposed computer-based system, since nodular lesion localization serves as an efficient process for the initialization of the subsequently applied active contour model. Figure 5 illustrates an example result of the application of the nodular lesion detection approach on a longitudinal US image.

3.3 Delineation of Thyroid Nodules

The considered delineation quality measure, applied for both manual and automatically derived delineations, is the overlap between the region A delineated by the algorithm and the "ground truth" region G, obtained by following the rule that a pixel belongs to a nodule when it is included in at least two out of the three manual delineations drawn by experts [28].

The inter-observer variability associated with the manual delineations is quantified by the coefficient of variation [29]. The values of the latter are found to range from 0.8 to 12.4% when considering the manual delineations obtained for each US image of the dataset, indicating



(a) (b) (c)

Figure 5. (a) Longitudinal US image of thyroid gland with a nodule, (b) ground truth thyroid nodule annotated by radiologists, and (c) classification result. The nodular tissues detected are coloured white.

the subjectivity affecting the experts' delineations. The average overlap of the delineations obtained by the utilized active contour is $92.3 \pm 4.2\%$. The utilized active contour obtains a minimum distance error of 1.4 ± 0.9 pixels, based on the ground truth derived from three experts' delineations. Figure 6 illustrates manual delineations for indicative thyroid nodule cases (Fig. 6(a_1)–(a_6)), in comparison to corresponding delineations as drawn by the active contour (Fig. 6(b_1)–(b_6)).

The application of the intensity-driven segmentation model [6] on the hypoechoic US images of the same dataset resulted in an average overlap of $91.3 \pm 3.6\%$ and a minimum distance error of 3.0 ± 1.4 pixels. These results indicate that the delineation quality of this model is comparable to the delineation quality of the texture-driven active contour utilized in the proposed approach in cases of hypoechoic thyroid nodules. However, the application of model [6] is limited to hypoechoic (and hyperechoic) cases, whereas the texture-driven active contour utilized in the proposed approach is capable of segmenting isoechoic thyroid nodules as well.

In [7], the hybrid multi-scale method proposed was experimentally evaluated using delineations performed by two individual experts on a dataset of 40 thyroid US images comprising both, hypoechoic and isoechoic nodules. The reported results in terms of average minimum distance error measured over the whole dataset are 2.5 ± 0.9 pixels and 2.2 ± 0.8 pixels, based on delineations of two individual radiologists. The application of the texture-driven active contour utilized on the proposed approach on US images of the available dataset resulted in an average minimum distance error of 1.3 ± 0.7 pixels.

A major drawback of the hybrid multi-scale method [7] is that it requires a-priori information about the shape of the nodule boundaries to be detected, utilizing the classic instance of the generalized Hough transform, which embeds the equation of a circle. This is very limiting for practical use as benign nodules most commonly have elliptical boundaries and malignant nodules exhibit boundary irregularities. Moreover, the hybrid-multi-scale model is based on an edge detection scheme which makes the whole process sensitive to US noise. On the contrary, the utilized active contour approach does not require any prior information about the shapes of the nodule boundaries, and the region-based formulation of the energy functional used contributes to noise-tolerant image segmentation.

3.4 Malignancy Risk Assessment

Experiments were performed for the classification of delineated thyroid nodules with respect to their malignancy risk, according to Tomimori's grading [5]. The utilized set of boundary descriptors includes LBP textural features, as well as shape features derived from CC histogram, CMP, and FD.

An SVM classifier [24] was used for the classification. In accordance with the recommendation in [25], 10-fold cross validation was performed for the generation of ROC curves. The resulting ROC curve is illustrated in Fig. 7, whereas the associated AUC is equal to 0.94 ± 0.02. It can be derived that for specificity equal to 0.90, the obtained sensitivity is 0.96. The current implementation of the proposed computer-based approach requires less than a minute for each thyroid US image, and is therefore applicable in

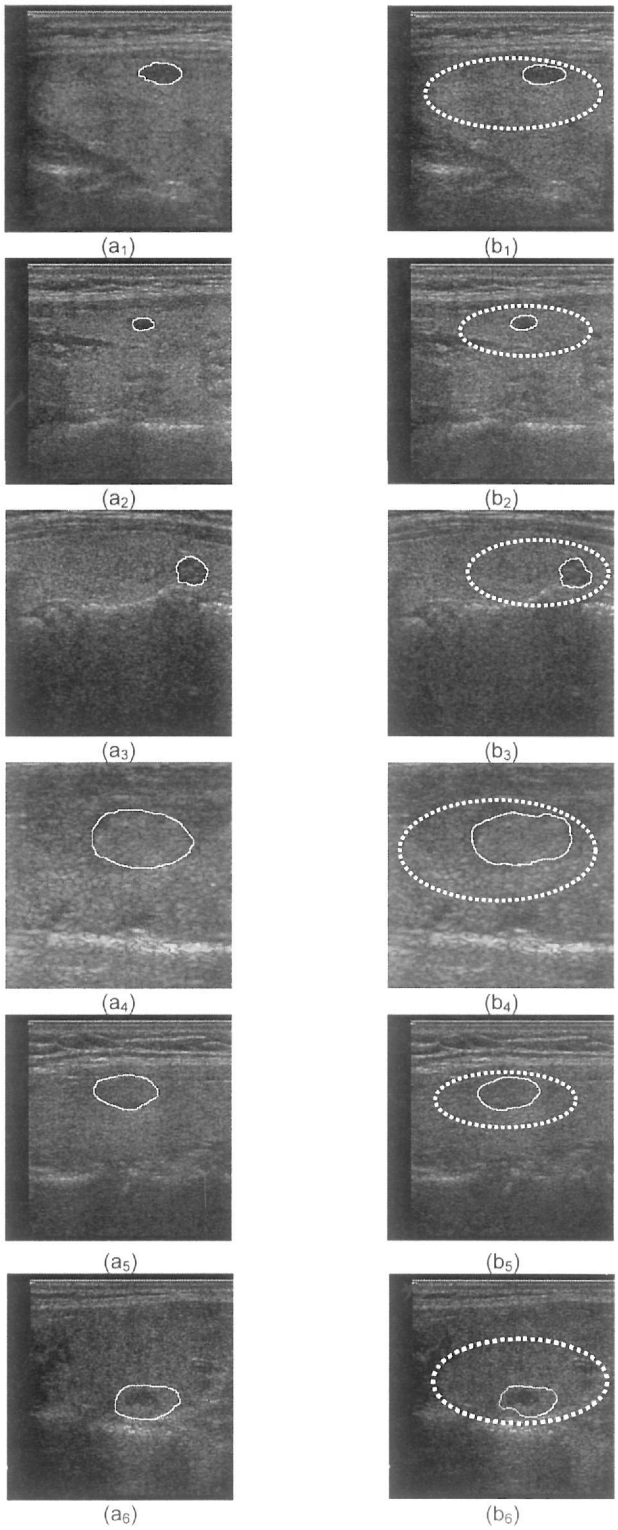


Figure 6. Two thyroid US images with delineated nodules: (a_1–a_6) manual delineations and (b_1–b_6) delineations obtained with the active contour. The initial contours are indicated with dashed lines.

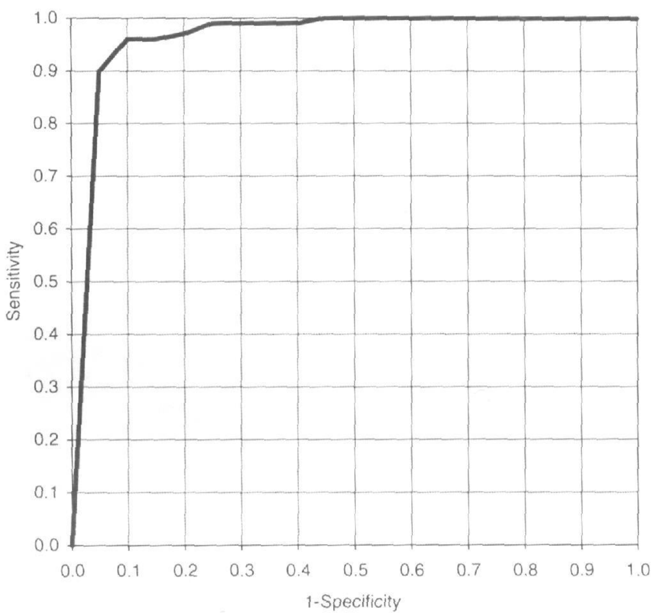


Figure 7. ROC curve obtained for the classification experiments.

clinical practice. In comparison, the co-occurrence matrix approach [10] obtains an AUC equal to 0.75 ± 0.06.

4. Conclusion

In this paper, we proposed a computer-based approach for the detection and malignancy risk assessment of nodules in thyroid US images. The proposed approach is automatic and integrates processes for the thyroid gland boundaries detection, the detection and localization of nodular lesions within the thyroid gland, the delineation of the detected nodules, and their malignancy risk assessment. The experimental evaluation on real thyroid US images, leads to the following conclusions:

- The manual delineations of the thyroid nodules indicate that the experts' subjectivity lead to noticeable inter-observer variability.
- Textural and shape features of thyroid nodules are capable of discriminating between low- and high-risk nodules, obtaining high sensitivity and specificity.
- The proposed computer-based approach requires less than a minute to perform nodule detection and malignancy risk assessment for each thyroid US image.
- The application of the proposed approach in clinical practice is feasible and could contribute to the objectification of the diagnostic process and the reduction of false medical decisions.

Future perspectives of this work include the following:

- Derivation of additional information from video frame sequences for the identification of thyroid nodules.
- Extensions for colour Doppler US images.
- Integration of heterogeneous information for the development of a medical decision support system for the identification of thyroid nodules.

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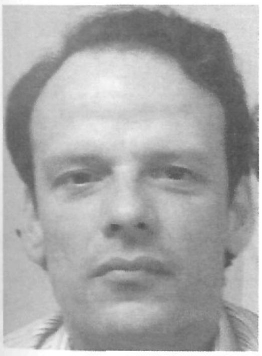
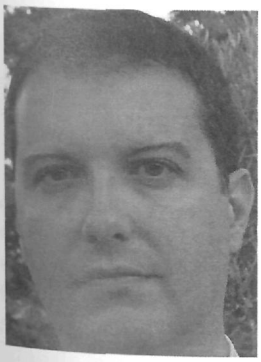


Ioannis Legakis is an Endocrinologist and currently has the position of the assistant director of the Department of Endocrinology and Metabolism in Henry Dunant Hospital in Athens, Greece. Moreover, since 2000, he collaborates with the University of Athens working on different aspects of endocrine pathophysiology and metabolism. He has participated in several local and international medical congresses and scientific meetings. Also he took part in scientific literature as an author and reviewer.



Michalis A. Savelonas received his B.Sc. degree in Physics in 1998, the M.Sc. degree in Cybernetics in 2001 with honors, and the Ph.D. degree in the area of Image Analysis in 2008 with honors, all from the University of Athens, Greece. He has co-authored 27 research papers and book chapters, whereas he has been actively involved in 7 European and National R&D projects. He is a reviewer in various international journals including Pattern Recognition and Signal Processing. Among positions in various academic institutions, which include University of Athens, Hellenic Air Force Academy and Technological and Educational Institute of Lamia, he is a research fellow in the Department of Informatics and Telecommunications, University of Athens, Greece. His research interests include image analysis, segmentation, pattern recognition, bioinformatics, and watermarking.

Dimitris Maroulis received his B.Sc. degree in Physics, the M.Sc. degree in Radioelectricity, the M.Sc. degree in Cybernetics with honors, and the Ph.D. degree in computer science, all from the University of Athens. He served as a research fellow for 3 years at the Meudon Observatory, Department of Spatial Sciences, France. Currently, he is an associate professor in the Department of Informatics and Telecommunications of the University of Athens. He has co-authored more than 120 research papers image/signal processing and analysis, real-time systems, and biomedical applications, and he is a reviewer in more than 10 international journals. He has been actively involved in more than 10 European and National R&D projects. His research interests include data acquisition and real-time systems, image/signal processing and analysis, and pattern recognition with applications on biomedical systems and bioinformatics.

Dimitris K. Iakovidis was born in Athens in 1973. He received his B.Sc. degree in Physics from the University of Athens, Greece. In April 2001, he received his M.Sc. degree in Cybernetics with honors and in February 2004 his Ph.D. degree from the Department of Informatics and Telecommunications, University of Athens, Greece. He has been working for over 10 years in the field of medical informatics and has been collaborating with many European hospitals and health centers as an expert on biomedical systems. Currently, among other academic positions, he holds a senior researcher position at the University of Athens, Greece. He has co-authored more than 80 research papers and book chapters, and he is a reviewer in 12 international journals, including IEEE Transactions on Image Processing, and IEEE Transactions on Biomedical Engineering. He has been actively involved in more than 10 European and National R&D projects. His research interests include image processing and analysis, data mining, pattern recognition with applications on biomedical systems and bioinformatics.