MITIS: a WWW-based medical system for managing and processing gynecological—obstetrical—radiological data

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- Gynecology
- Internet-based systems
- Telemedicine
- ISAPI
- DICOM
- Segmentation
- Classification
- Registration

**Summary** In this paper a World Wide Web (WWW)-based medical system, called MITIS, is designed and developed for the management and processing of obstetrical, gynecological and radiological medical data. The system records all the necessary medical information in terms of patient data, examinations, and operations and provides the user-expert with advanced image processing tools for the manipulation, processing and storage of ultrasound and mammographic images. The system can be installed in a hospital’s Local Area Network (LAN) where it can access picture archival and communication systems (PACS) servers (if available), or any other server within the radiology department, for image archiving and retrieval, based on the digital imaging and communication in medicine (DICOM) 3.0 protocol, over TCP/IP and also it is accessible to external physicians via the hospital’s Internet connection. MITIS is composed as a set of independent WWW modules (ISAPI server extension dlls) and a Win32 application (COM+ server) for mammography image processing and evaluation. © 2004 Elsevier Ireland Ltd. All rights reserved.

**1. Introduction**

It is widely recognized that the World Wide Web (WWW) has become the major infrastructure for giving access to sophisticated applications from virtually any machine and operating system, allowing all users to communicate at distance by relying on a common application server. In the medical field, many telemedicine application based on the Web utilize a standardized technical solution according to which all information and applications are stored in a locally centralized location and they can be distributed over a network in several clients. The use of a standardized communication platform resulted in the development of various Web-based medical systems, which offer new telemedicine services on a number of different medical cases [1].

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In particular, medical image viewing systems have been developed over the past years based on the Internet and the ubiquity of the Web browser. A complete and secure Internet-based system, called JReads, has been developed for viewing medical images consisting of a Java applet at the front-end, JReads, and relational databases and image files servers at the back-end [2]. In [3], a system was introduced using WWW technologies and HTTP communication protocols for remotely processing ultrasound images by using the Angle Independent Doppler Color Image algorithm and by providing several image measurements through various Internet tools. Furthermore, another telemedicine system was also introduced in [4] providing telemedicine services for radiotherapy treatment planning whereas in [5], a telemedicine system, called KAMERIN, has been developed for supporting cooperative work and remote image analysis of radiological data for ISDN-based telecommunication.

The implementation of the aforementioned systems was based on the acceptance of a standard medical image communication protocol, known as digital imaging and communication in medicine (DICOM) [6], as well as on the development of picture archival and communication systems (PACS) for handling and storing the image data generated by various medical modalities [7]. These WWW-based systems involve mainly medical experts from Radiology Departments. On the other hand, there is a strong need for incorporating experts from other departments and/or hospitals throughout such systems like experts from the Obstetric and Gynecology departments. In the bibliography, only a few research works have been focused on the use of the Internet technology for obstetrical and gynecological purposes [8–10]. In these papers, the authors mainly addressed the available equipment and technologies as well as the possibilities of delivering new services throughout the Internet without implementing those technologies towards the development of WWW-based systems for handling obstetrical and gynecological data.

In this paper, we have developed a complete and secure WWW-based system for the management and processing obstetrical, gynecological, and radiological medical data. The proposed system hereafter is called MITIS, from the name of the ancient goddess of Greek mythology considered as a goddess of prudence. The system is a set of independent modules, connected with each other and fully compatible with the WWW, thus, providing flexibility and extensibility. It records all the necessary information related with different patient’s examination, operation, and any other gynecological data related with woman’s pregnancy and labor. It also incorporates computer graphics algorithms and advanced digital image processing techniques for manipulating various medical images including ultrasound and mammographic data. An advantage of the system is the provision to the medical experts of a unified patient management mechanism, either in the hospital or outside. Furthermore, it offers cooperation of medical specialists from different medical departments such as the obstetrics–gynecology department and the radiology department either within the hospital and/or between hospitals or private offices towards the monitoring of the progression of a disease and the establishment of a therapeutic scheme.

2. Methods and materials

2.1. General MITIS system structure

Fig. 1 shows the functional structure of the MITIS system. The system is a WWW-based medical information system based on three-tier client-server architecture and designed to provide mainly gynecologists with unified patient management capabilities, either internal in the hospital or external at a private office. According to Fig. 1, the MITIS server is originally installed in a hospital and, via Internet connection, it is accessible to other external physicians. On the server side, the system, via the Local Intranet Network (LAN) of the hospital, can access the hospital’s PACS servers (if available), or any other server within the radiology department for image archiving and retrieval, based on the DICOM 3.0 protocol, over TCP/IP. External physicians access MITIS via Internet, mostly via Point-to-Point Protocol (PPP) dialup connections (PSTN or ISDN of 64kpbs). These external physicians can be located in the same city, in rural villages or islands and they can share the same patient information with the hospital. Thus, the MITIS system can serve two roles as: (a) a patient medical record management system, and (b) a system supporting telemedicine sessions either of different examinations and operations or remote medical image processing.

2.2. MITIS system architecture

Fig. 2 depicts the overall MITIS system architecture which follows the three-tier model: HTML pages with client-side Javascripts and xmi data islands in the front end, Internet Server Application Program Interface (ISAPI) extensions (dlls) combined with Microsoft Active Server Pages (ASP) in the middle-tier.
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and a RDBMS with available ADO drivers (Microsoft SQL Server 2000 preferable) at the back-end. The MITIS system operates under Microsoft Windows NT/IIIS 4.0 or 2000/IIIS 5.0 or newer platforms.

The MITIS system was designed by making use of existing advanced Internet technologies and tools. Since one of the main requirements of the MITIS system was the compatibility with WWW technologies,
alternative scenarios of existing technologies along with combination with other supporting tools were initially evaluated. Table 1 depicts the technological scenarios, as well as criteria and scoring. From those criteria, the integration with other technologies refers to the integration with Win32 API services, while the development productivity is a combination of the level of expertise of the development team and the availability and cost of the development tools.

According to Table 1, the first solution of Microsoft Active Server Pages, connected with a database throughout ADO, supports Component Object Model (COM) technologies, but it presents medium performance and development productivity. The PHP: Hypertext Preprocessor, connected with a database throughout ODBC, presents the same disadvantages with ASP and furthermore limited integration with operating system and external services. The Internet Server Application Program Interface extensions with middle tier COBRA, using AT&T’s omni as ORB, have the disadvantage of low development productivity due to its minimal support by RAD tools such as Microsoft Visual Basic, Delphi, etc. The replacement of the ORB omni with other commercial product of Borland such as the VisiBroker, may offer a significant improvement in development productivity with the disadvantage of a high deployment cost. The implementation of the Client Side ActiveX, even though it increases the performance of the system, it increases the bandwidth requirements considerably due to higher network traffic, it requires more computational power from the client (thick client) and it is exposed to higher security threats (distribution and installation of ActiveX components only). The option of using Java Applets/JavaBeans components to develop such system as the proposed was seriously consider for the particular application but it was finally rejected due to the higher level of expertise of the development team in the Win32 application and the better integration capabilities of the latter with Win32 API services. For similar reasons the Java Servlets/Java Server Pages (JSP) were also excluded. Microsoft .NET platform is a very promising solution but it was not fully available at the time of the development of the proposed system. For all the aforementioned reasons, the MITIS system was finally based on a mixture of the ISAPI extensions (dlls) and ASP. This technology, available by Borland, is initially developed for Delphi and it is named as Websnap.

MITIS is composed of a set of independent WWW modules (ISAPI server extension dlls) and a Win32 application (COM+ server) for mammography image processing and evaluation. The modules, that

<table>
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<tr>
<th>Criteria</th>
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<th>ASP</th>
<th>ISAPI extensions with ADO</th>
<th>ISAPI extensions with OMNI</th>
<th>Client side ActiveX</th>
<th>Java Applets/JavaBeans</th>
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</table>

Table 1: Comparison of WWW technologies for the development of the proposed MITIS system in terms of specific criteria.
have been developed throughout the MITIS system, along with a description of the data supported by these modules. In terms of managing various examinations and diseases, are then presented.

2.2.1. Basic control module
This module controls the user authentication, the display of persistent session info, the construction of the menu and the system’s login page. The module is declared in a simple XML file, which can be easily edited with a text editor. Also, in this module, an electronic scheduling tool is incorporated to manage all patient examinations. Furthermore, all the predefined parameters related to various medical examinations and operational findings, imported prior to the system, are configured throughout this module.

2.2.2. General data module
This module supports all patients’ general data, including past medical history (individual and hereditary), habits, allergies, drugs, etc. The patient’s medical history data as well as the diagnostic data were coded according to the International Classification of Diseases (ICD-10) protocol.

2.2.3. Patient examinations module
This module keeps record of all medical examinations including obstetrical, gynecological, clinical breast examinations, laboratory and radiological examinations. Throughout this module, the user can have access to the information related to any aforementioned examination including diagnostic information, in a parameterization manner, pharmaceutical treatment required and/or any other specific medical instruction.

2.2.4. Obstetrical examination module
This module manages all the obstetrical examination data. It contains all the necessary data related to the woman’s pregnancy and labor. In particular, the module supports parameters during pregnancy and the labor such as examinations of the placental, systolic and diastolic arterial pressure, weight and temperature of the pregnant, dates of the duration of pregnancy, type of labor, number of fetuses, parameters of the fetus clinical examination, recording of problems related with the pregnancy and the labor, bone density measurements, etc. Furthermore, this module is connected with radiological test examinations module, and it controls the image data related to any ultrasound examination.

2.2.5. Gynecological examination module
This module manages all the gynecological examination data. It contains all the necessary information related to the clinical examination of gynecological organs such as cervix, uterus, fallopian tubes, ovaries, etc. Also, the module controls all clinical data related to any abdominal wall examination and vaginoscopy.

2.2.6. Gynecological operation module
The module records the history of all gynecological operation per patient based on the name of the patient and date of her operation along with all the corresponding clinical findings. The information controlled by this module includes type and description of each operation, operational schemes (frontal anatomical, oblique anatomical, operational incisions, external gynecological organs), pathological findings of fallopian tubes and ovaries, information related to possible implications, etc. The specific module also includes four different graphical ‘notebooks’, which are developed by implementing computer graphics algorithms and they correspond to the aforementioned four types of operational schemes. Through these graphical ‘notebooks’, the expert could easily draw and/or locate predefined operational findings such as inflammation, cyst, malignant, fibromyoma, endometriosis, lymph node, and symphysis.

2.2.7. Laboratory examinations module
The specific module records the results of various laboratory examinations including blood tests, biochemical blood tests, urine tests, urine tests culture, vagina fluid examination, stool test, hormonal examinations, ions, cancer and hepatic markers, etc. All the laboratory examination parameters were coded using the ICD-10 protocol. In Fig. 3, a typical screen of the major ions and cancer and hepatic markers recorded within the MITIS system is shown.

2.2.8. Pap Smear module
The module controls all the estimates related with the gynecological Pap Smear, a test used for the early diagnosis of cancer of the uterus.

2.2.9. Clinical breast examination module
This module holds all the information related to any clinical breast examination. It includes reasons for the specific examination, breast review (breast asymmetry, location, breast color, nipple status, etc.), breast palpation (location of a mass, characterization of the mass, etc.), pathological breast examination (excision, biopsy) and supplementary measurements (temperature, systolic and diastolic arterial pressure, etc.).
2.2.10. Radiological test examination module
This module provides access to all data acquired from any medical image modality within the hospital. It implements the appropriate communication interfaces to the external systems such as PACS of the hospital or any other medical image archiving system located at the radiology department and it is connected with the system’s image processor for displaying, manipulating, and processing the data. Throughout this module, the system currently processes ultrasound and mammographic images in DICOM format.

2.3. MITIS system functionality
The development of the MITIS system, in terms of interface, is focused towards the medical expert—user, it supports a number of users at the same time, and it is user friendly, requiring only knowledge of the Microsoft Windows environment. The main functionalities of the MITIS system are:
(a) management of the patient data, and (b) image processing and visualization of various gynecological data.

2.3.1. Management of patient data
The patient medical record is organized in three levels: (a) Patients, (b) Visits, and (c) Various Examinations—Operations. The latter contains patient data related with various examinations (Blood tests, Radiological examination, Clinical Gynecological–Obstetrical examination, Breast examination), other examinations (Pap Smear, Mammography, Sperm examination), and Surgical Operations–Deliveries. The main data recorded in those examinations were described in the previous section along with the system’s modules.

It must be pointed out that the MITIS system offers a variety of capabilities for searching a specific patient, obtaining her list of all examinations and operations, sorted by date, and producing specific reports for each patient with all her clinical history. Another advantageous capability of the system is the prior input of vast gynecological information in a coded manner and the completion of the results of each examination form with simple selections (use of look-up tables) by the user. Furthermore, the user can make any change in this predefined information by using specific tools provided by the system.

2.3.2. Image processing and viewing of gynecological data
This image processor provides all the capabilities for manipulating any gynecological images within the database (images in DICOM format), including image acquisition, display, image saving capabilities in different image format and image process-
2.3.2.1. Image enhancement tool. It includes a filter for histogram equalization, unsharp masking (Laplacian of a Gaussian), and the contrast limited adaptive histogram equalization (CLAHE) [11].

2.3.2.2. Image segmentation tool. This tool provides the specialist with the ability to isolate Regions of Interest (ROIs), both manually and automatically.

Methodology. According to the automatic approach, the segmentation of specific ROIs of mammographic images is performed by the development of a new algorithm based on mathematical morphology [12] applied in mammographic images. The proposed new segmentation algorithm is stated as follows:

1. For a predefined circular structuring element, with radius \( R \):
   \[
   r_{\text{enh}}^b = I - (I \ominus B) \ast \text{rec} \tag{1}
   \]
   where \( I \) is the original image, \( B \) a circular structuring element with radius \( R \), \( \ominus \) is the morphological opening operation defined by: \( (I \ominus B) = (I \oplus B) \ominus B \) with \( \oplus \) and \( \ominus \) denoting the morphological operations of erosion and dilation, respectively, and \( \ast \text{rec} \) the operation of the opening by reconstruction of erosion [13].

2. Creation of a binary image, \( I_{\text{bin}}^b \), after thresholding, according to the following operation:
   \[
   I_{\text{bin}}^b = \text{THR}(r_{\text{enh}}^b, t) \tag{2}
   \]
   where \( \text{THR}(\cdot) \) is the thresholding operation at level \( t \), which can be calculated by the histogram of the \( r_{\text{enh}}^b \) image.

3. Contour extraction of the ROI, by applying the following morphological operation [14]:
   \[
   \text{Contour} = r_{\text{bin}}^b - (I_{\text{bin}}^b \ominus W) \tag{3}
   \]
   where \( \ominus \) denotes the erosion operation using a \( W \) structuring element with size 3 x 3 pixels.

According to the aforementioned algorithm, initially the original image is processed by a morphological opening operation. This operation results the removal of regions with size less or equal to the size of the structuring element used. Then, the operation of opening by reconstruction of erosion is applied which reconstructs only the removed regions from the application of the opening operation. By subtracting the result image from the original, an enhanced image of the surrounding area of the specific ROI is then obtained. The thresholding process is also applied to create a binary image of the ROI followed by the morphological contour algorithm in order to isolate the boundary of the ROI. The same processes could be repeated using structuring elements of different radius \( R \in [R_1, R_2] \) in order to detect ROIs of the original image with different sizes and to create a final image where all ROIs are pasted.

Experimental results. The presented automatic algorithm was successfully applied to a number of pathological mammographic images where tumors like ROIs were automatically segmented. Typical result of the application of the proposed segmentation algorithm is shown in Fig. 4. Fig. 4a displays an initial mammographic image containing a suspicious area (possible tumor) which has to be extracted. Initially, an opening operation is performed with a circular structuring element of radius 15 pixels, as shown in Fig. 4b, which results the suppression of structures with size less or equal to the size of the structuring element used. Then, the operation of opening by reconstruction of erosion is applied using the same size of the structuring element, which reconstructs the information suppressed by the application of the opening operation (see Fig. 4c). By subtracting the image of Fig. 4c from the initial image, an enhanced image around the area of the tumor is obtained and displayed in Fig. 4d. By applying the thresholding operation, with value of 60 gray levels for the specific case, the ROI of interest is obtained as shown in Fig. 4e. Finally, the application of the morphological contour extraction operation results an 1 pixel width contour of the ROI as shown in Fig. 4f superimposed on the initial mammographic image. In cases where multiple ROIs have to be extracted within the same image, the aforementioned process of Step 1 is repeated using different size of circular structuring elements sequentially applied, with radius varying from 3 to 18 pixels, until all the ROIs to be obtained.

The proposed automatic algorithm for extracting ROIs (such as tumors) of mammographic images was tested against two other segmentation algorithms based on mathematical morphology that are broadly used in various clinical applications. The first algorithm is the top hat filtering method, which is based on use of simple morphological operations in order to separate tumor from surrounding noise [15]. The algorithm consists of the following steps:

(a) application of a morphological opening operation, (b) subtraction of the opened image from
Fig. 4 Segmentation of pathological mammographic images. (a) The initial mammographic image. (b) The result of the opening operation on the initial image. (c) The result of the opening by reconstruction of erosion. (d) The difference image. (e) The isolation of the ROI, after thresholding. (f) The extracted contour of the ROI superimposed on the initial image using the proposed automatic morphological-based segmentation algorithm. (g) The extracted ROI of the initial image using the top hat filtering segmentation method. (h) The extracted ROI of the initial image using the watershed transformation segmentation algorithm.
the original image, (c) thresholding (according to Eq. (2)), and (d) contour extraction (according to Eq. (3)).

The second segmentation algorithm is based on the application of the watershed transformation [16]. According to this methodology, the mammographic image is considered as a 3D topographic surface. The intensity of each pixel denotes the elevation in the corresponding location. The objective of this transformation is to find the watershed lines in topographic surfaces. Each local minimum of the surface is considered as an initial point for a flooding process, which begins from those points and raises until it reaches the flooding of another adjacent minimum. The boundaries of the created adjacent regions are the results of the segmentation process.

In Fig. 4g and f, the results of the application of the top hat filtering method and the watershed transformation on the same mammographic image of Fig. 4a are shown, respectively. Comparing these results with the extracted ROI of Fig. 4e, it can be seen that both algorithms, top hat filtering method and watershed transformation, are over-segment the specific ROI, in comparison with the proposed automatic segmentation algorithm, since artifacts are attached to the extracted ROIs derived from the surrounding tissues.

Furthermore, a comparative quantitative analysis of the results obtained from the application of the three segmentation algorithms for 20 selected mammographic images was also performed. The results of the algorithms were compared against ideal contours manually drawn by an experienced specialist. The comparisons were based on the calculation of the distance of the each contour obtained by the three segmentation algorithms from the manually defined contour. Initially, a distance map of the manually obtained contour is calculated according to which a value equal to its Euclidean distance from the closest point of the contour is assigned to each pixel. A fast calculation of the city block distance map can be found in [17]. Then, the average distance between the two contours is calculated by averaging the values of the one contour over the values of the distance map calculated from the other contour according to the following equation:

$$\text{Dist}(C_1, C_2) = \frac{1}{n} \sum_{(x,y) \in C_1} \text{DM}_{C_2}(x,y)$$

<table>
<thead>
<tr>
<th>Image</th>
<th>Average distance (in pixels)</th>
<th>The proposed segmentation algorithm</th>
<th>Top hat filtering algorithm</th>
<th>Watershed transformation algorithm</th>
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</table>
where \( C_1 \) is each contour extracted by the three segmentation algorithms, \( C_2 \) the manually obtained contour by the expert, \( DM_{C_2} \) is the distance map of the \( C_2 \) contour and \( n \) is the total number of \( C_1 \) contour points. According to Eq. (4), the similarity of the two compared contours increases as the value of the average distance becomes lower.

Quantitative results of the application of the three segmentation algorithms are presented in Table 2. It can be seen that the value of the average distance (in pixels) of the contour points obtained by the proposed morphological algorithm from the corresponding manually obtained contour points is always lower than the values of the average distances of the contours obtained by the top hat filtering method and the watershed transformation algorithm for all test images. Also, the watershed transformation outperforms compared to the top hat filtering method. These results reveal the advantageous performance of the proposed automatic segmentation algorithm over the two other segmentation algorithms in terms of accuracy.

Moreover, the proposed automatic segmentation algorithm consists of an optimal modification of the top hat filtering method by incorporating the morphological opening operation by reconstruction of erosion, which preserves the shape of the features that are not removed by the erosion. Thus, the opening by reconstruction of erosions extracts the ROI while eliminates surrounding artifacts, which remain present by applying the top hat filtering method. Also, the application of the watershed transformation in mammographic images results an over-segmentation of the images due to the existence of high frequency distortions. In order to correct this problem, in our implementation, a set of initial markers is manually defined. As a result, the segmentation of mammographic images in a clinical environment becomes less practical than the proposed automatic segmentation algorithm.

The automatic algorithm was applied to a number of pathological mammographic images (see Section 2.3.2.3) and failed to segment regions surrounded by fat tissue or microcalcifications, even though the aforementioned enhancement filters were applied prior the segmentation process. In those cases, and since the whole system is addressed to experts in their every day practice, a manual method is also provided.

2.3.2.3. Classification of mammographic images.

In the MITIS system, a decision support system was also developed and incorporated within the whole telemedicine system. The module is a classification system of mammographic images and a block diagram of the classification process is shown in Fig. 5. According to the diagram, each mammographic image is firstly processed by the image processor in order specific ROIs to be extracted, either automatically or manually. Then, the ROIs are further processed by the classification module. The classification module comprise of two sub-modules: the feature extraction module and the classifier. It must be pointed out that the classification module in its present implementation classifies segmented ROIs to two predefined classes: pathological and normal regions from the numerous pathological cases related to the mammography.

The feature extraction module. The feature extraction module assigns to each segmented ROI of the mammographic image features that quantitatively describe this region. Five different feature extraction methods were evaluated in terms of classification rate: (a) Features of the First-Order Statistics [18], (b) Features of the Second-Order Statistics [19], (c) Features based on Wavelets [20], (d) Features based on Law Masks [21], and (e) Features based on Fractal Theory [22].

The classifier. The classifier consists of a multi-layer feedforward Artificial Neural Network (ANN) comprising of two layers of neurons, the input and output layers [23]. The input layer consists of a number of neurons equal to the number of the extracted features. The output layer consists of one neuron, encoding the two classes of the subjects: pathological and normal ROIs (0, pathological; and 1, normal). The back-propagation algorithm with

![Fig. 5 Block diagram of the MITIS decision support system for the classification of mammographic images.](image-url)
adaptive learning rate and momentum has been used in order to train the ANN [20]. The initial weights of the neurons have been randomly selected in the range $[-1.0, +1.0]$. The log-sigmoid and tan-sigmoid activation functions have been used for the hidden and the output layer, respectively. The values of the learning rate and the momentum have been estimated using a process of trial-and-error until no further improvement in classification could be obtained. In order to avoid overtraining and achieve an accepted generalization in the classification, three data sets have been selected: training set, validation set, and testing set. The ANN is trained using the training set and the training phase stops when the performance in the validation set is maximized.

Test mammographic data. Three hundred and thirteen mamographic images (205 normal and 108 pathological) were used for the evaluation of the classification module. These images were selected from the MiniMammography Database of the Mammographic Image Analysis Society, containing 320 digitized films, each of 1024 × 1024 pixels and 256 gray levels (8-bits) [24]. The 313-mamographic images involved in the present study were finally chosen after thorough inspection by an experienced radiologist. All mammographic data used in the study were in Portal Grey Map (PGM) format. The data available were partitioned into three disjoint data sets: the training set consisting of $0.6 \times 205 = 123$ normal and $0.6 \times 108 = 65$ pathological ROIs, the validation set consisting of $0.2 \times 205 = 41$ normal and $0.2 \times 108 = 22$ pathological ROIs, and the test set consisting of $205 - 123 = 41$ normal and $108 - 65 = 22$ pathological ROIs. Furthermore, all images were processed by the user-doctor using the image processor for the enhancement of the images and the extraction of ROIs. From the 108 pathological images, 85 ROIs were successfully extracted automatically by the module, whereas the rest 23 ROIs were further processed with the manual method. The diameter of the pathological ROIs was $62 \pm 32$ pixels (mean value ± standard deviation). The expert manually selected similar size of ROIs from the normal mammographic images.

Experimental classification results. During the experimental phase, neural networks with different number of neurons in the hidden layer were tested. The results of the classification process, in terms of the best classification rate achieved by each feature extraction method, are presented in Table 3. These results clearly show that the use of the features of the Second-Order Statistics outperformed compared to any other feature extraction method implemented in this study. According to these findings, the final classification module incorporates a neural network classifier with a hidden layer of five neurons and an output layer encoding two classes (normal, pathological). The features that form the input vector of the classifier were the following: Angular Second Moment, Contrast, Correlation, Variance, Inverse Different Moment, Sum of Squares, Sum of Variance, Entropy, Sum of Entropy, Entropy Variance, Correlation Information Measures, resulting a final feature vector with dimensionality of 48.

<table>
<thead>
<tr>
<th>Feature extraction methods</th>
<th>Classification rate (best correct results)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of neurons</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>First-order statistics</td>
<td>10</td>
</tr>
<tr>
<td>Second-order statistics</td>
<td>5</td>
</tr>
<tr>
<td>Wavelets</td>
<td>10</td>
</tr>
<tr>
<td>Law masks</td>
<td>25</td>
</tr>
<tr>
<td>Fractal theory</td>
<td>20</td>
</tr>
</tbody>
</table>

2.3.2.4. Registration of mammographic images. Another image processing capability offered by the system is the registration of mammographic images (in DICOM format). The purpose of this application is mainly the evaluation of a therapeutic scheme and/or the comparison of the two breasts in terms of pathology.

Methodology for registration of mammographic images. The specific methodology concerns with the implementation of two registration methods: (a) the manual method, by the placement of corresponding points between the two images to be registered, and (b) the automatic method, which is
based on the automatic extraction of the external breast boundaries.

Manual registration: According to manual registration the user defines $K$ pairs of corresponding points (markers), one on the reference image and one on the image to be registered, that correspond to the same anatomical structure, by using the MITIS software. The problem of registering the two images becomes one determining the geometric transformation that spatially aligns the pairs of corresponding markers. The problem of determination of the transformation parameters can be defined as one of solving two linear systems. The linear system can be stated in mathematical form as $B_A = c_i$ for $i = 1, 2, \ldots$, for $x$- and $y$-axis, respectively, where $B$ is a matrix of size $3K \times K$, holding the coordinates of the corresponding markers before registration, $A_i$ is a vector of size $3K \times 1$, holding the parameters of the geometric transformation used, and $c$ is a vector of size $2K \times 1$ that holds the coordinates of corresponding points in the reference image.

The geometric transformation selected was the 2D affine transformation, which is able to model most of the possible movements of the anatomical structure of interest, by introducing the lowest possible complexity. The affine transformation is defined in mathematical terms as follows:

$$\begin{pmatrix} x' \\ y' \end{pmatrix} = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix} + \begin{pmatrix} a_{10} \\ a_{20} \end{pmatrix}$$ (5)

The affine transformation is controlled by six independent parameters ($N = 6$), which allow independent translation rotation and scaling in each cartesian axis.

The linear system is solved employing Least Squares Approximation (LSA) to minimize $e^T e$, where $e = B_A - c_i A_i = (B^T B)^{-1} B^T c_i$, while the transpose of $B$ is calculated using Singular Value Decomposition [25]. From the above analysis, it becomes obvious that in the case of $N = K$ (e.g. six fiducial markers if the affine transformation is employed), the distance between the fiducial markers on the reference and the transformed image is zero. As the number of markers increases, this distance becomes non zero by minimal.

Automatic boundary-based registration: This approach is based on the automatic identification and the spatial coincidence of the breast boundaries of the reference image and the image to be matched similar to [26]. It does not require the intervention of the user and can be encoded into the following steps:

1. Breast boundary extraction from the pair of images to be spatially registered based on the application of the contrast limited adaptive histogram equalization operation [11], followed by a thresholding operation and the application of the morphological contour extraction operation according to Eq. (3).

2. The distance transform ($DT(M_0)$) of the breast boundaries of the reference image is produced. The distance transform accepts as input a binary image and produces as output a 2D float image, each pixel of which holds the distance of the specific pixel from the closest non zero pixel of the input image. The resulting float image is called Distance Map (DM) and a very fast implementation can be found in [17].

3. The affine geometric transform is applied on to the image to be registered to match it spatially with the reference image.

4. The parameters of the affine geometric transform $T$ are determined by the application of the Simulated Annealing (SA), hybridized by the Powell conjugate method [27], using the following Measure of Match (MM) between the reference image and the image to be registered:

$$MM = \sum_{x,y \in M_1} DT(M_0(x,y)) T_A(M_2(x,y))$$ (6)

where ($DT(M_0)$) is the distance transform of the reference image, $T_A$ is the transformation matrix over the $M_2$ image to be registered.

5. The affine transformation that was determined by spatially coinciding the breast boundary is applied to the whole second image.

Experimental registration results. The two aforementioned registration techniques (the marker-based manual and the breast boundary-based automatic techniques) have been applied to 12 pairs of mammographic images. The images from each pair were acquired from the same woman at different times. A radiotherapy expert performed the marker placement for the manual method. In Fig. 6, results of the manual and automatic boundary-based registration techniques are presented. Both registration methods seem to perform relative satisfactory.

For the quantitative assessment of the two registration techniques, the absolute value of the correlation coefficient was used, calculated between the reference image and the registered image. The absolute value of the correlation coefficient is independent of linear changes in brightness between the two images and is a measure of the spatial coincidence of the two images to be registered. The measure of match of the individual techniques was excluded to avoid biased results of the comparison.
MITIS: a WWW-based medical system for managing and processing

Fig. 6 Registration of mammographic images. (a and b) The reference mammographic image and the image of the same patient at different time to be registered along with the placement of markers by the expert. (c and d) The transformed image and its boundary superimposed on the reference image using the manual registration technique. (e and f) The transformed image and its boundary superimposed on the reference image using the automatic boundary-based registration.
Generally, in the case of two images $I_1 : S_1 \rightarrow \mathbb{Z}$ and $I_2 : S_2 \rightarrow \mathbb{Z}$, where $S_1, S_2 \subseteq \mathbb{Z}^2$, $\mathbb{Z}$ is the set of integers, that intersect over $S = S_1 \cap S_2$, the correlation coefficient $\text{CC}(I_1, I_2)$ is defined by the following relation:

$$
\text{CC}(I_1, I_2) = \left\{ \sum_{(x_1, x_2) \in S} \left( I_1(x_1, x_2) - \bar{I}_1 \right) \left( I_2(x_1, x_2) - \bar{I}_2 \right) \right\} / \sqrt{\sum_{(x_1, x_2) \in S} (I_1(x_1, x_2) - \bar{I}_1)^2} \times \sqrt{\sum_{(x_1, x_2) \in S} (I_2(x_1, x_2) - \bar{I}_2)^2}
$$

where $\bar{I}_1$ and $\bar{I}_2$ are the average values of the grey levels of the two images calculated for the points $(x_1, x_2) \in S$.

The results of the application of the two aforementioned registration techniques to 12 pairs of mammographic images are presented in Table 4. The Student’s paired $t$-test was applied along with the predefined findings/diseases using a graphical interface (Fig. 8c), and the radiological test examination along with a typical ultrasound image from the hospital’s PACS in DICOM format.

### Table 4 Absolute values of correlation coefficient for 12 pairs of clinical mammographic images using the manual marker-based registration and the automatic boundary-based registration techniques

<table>
<thead>
<tr>
<th>Image pairs</th>
<th>Absolute values of the correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Manual registration</td>
</tr>
<tr>
<td>Pair 1</td>
<td>0.7629</td>
</tr>
<tr>
<td>Pair 2</td>
<td>0.7499</td>
</tr>
<tr>
<td>Pair 3</td>
<td>0.7995</td>
</tr>
<tr>
<td>Pair 4</td>
<td>0.8184</td>
</tr>
<tr>
<td>Pair 5</td>
<td>0.8090</td>
</tr>
<tr>
<td>Pair 6</td>
<td>0.8167</td>
</tr>
<tr>
<td>Pair 7</td>
<td>0.7667</td>
</tr>
<tr>
<td>Pair 8</td>
<td>0.7425</td>
</tr>
<tr>
<td>Pair 9</td>
<td>0.7759</td>
</tr>
<tr>
<td>Pair 10</td>
<td>0.8090</td>
</tr>
<tr>
<td>Pair 11</td>
<td>0.8184</td>
</tr>
<tr>
<td>Pair 12</td>
<td>0.7629</td>
</tr>
</tbody>
</table>

2.4. **MITIS system security**

The first step to establish secure communication was the use of a password-based user authentication. Apart from this common username/password combination, the compatibility of MITIS with WWW permits the adoption of open and reliable user authentication and encryption technologies such as Secure Sockets Layer (SSL) to provide secure communication channel between the server and clients. The SSL is a standard protocol for secure WEB transactions and it operates on the basis of public and private keys.

Furthermore, Microsoft Windows 2000/NT 5.0 was installed on MITIS system to improve security of Windows. All resources were placed on the Windows NT File System (NTFS). User verification procedure was based on both a users information database in the server and digital certificates from a mutually trusted third-party organization, such as VeriSign (http://www.verisign.com). Users are unable to access the programs unless they provide both correct login information and their digital certificates.

3. **Clinical results**

**MITIS** is a WWW-based system that is designed and developed for managing patient data from various examinations including obstetrical, gynecological, clinical breast examinations, laboratory and radiological test examinations in a very user friendly manner, requiring only basic knowledge of the Windows-type environment from the user-medical experts.

The user-expert can access the main WEB-page of the MITIS system, through a username/password. He (or she) can choose any application provided by the system through the menu. The system provides two ways of navigating: either through the main menu at the top of the specific application window or by using a floating toolbar placed anywhere in the desk top, offering access to all MITIS system capabilities. Fig. 7a shows a typical WEB-page of the patient data along with the main menu marked, whereas Fig. 7b shows the MITIS floating toolbar. Also, Fig. 8 shows the typical WEB-pages for a gynecological examination (Fig. 8a), a pregnancy/labor monitoring examination (Fig. 8b), the frontal operational scheme applied along with the predefined findings/diseases using a graphical interface (Fig. 8c), and the radiological test examination along with a typical ultrasound image from the hospital’s PACS in DICOM format.
MITIS: a WWW-based medical system for managing and processing medical images

Fig. 7 (a) Typical WEB-page of recording patient data along with the main menu (marked). (b) The MITIS floating toolbar.

Fig. 9 displays typical WEB-pages for the application of the developed image processing algorithms. Specifically, Fig. 9a shows an isolated ROI within a mammographic image (locations and dimensions in pixels) along with the result of the classification process (normal, pathological) according to the decision support system. In the specific figure, the expert selected a ROI, which then is passed to the decision support system classifying the ROI as normal. Since the installation of the MITIS system in a clinical environment, the classification module was further tested for the classification of 40 mammographic images; 20 of those were characterized as normal and the rest pathological, according to the specific clinical examinations. The classification module was able to correctly distinguish 18 out of the 20 (classification rate 90.0%) as normal and 16 out of 20 as pathological (classification rate 80.0%), as shown in Table 5. Thus, during the clinical implementation of the MITIS system, a total 85.5% of classification rate has been achieved throughout the classification module for both categories.

Also, Fig. 9b displays to the expert a representative result of the registration of mammographic images.
Fig. 8 Typical WEB-pages for: (a) The gynecological examination. (b) The pregnancy/labor monitoring. (c) The frontal operational scheme applied along with the predefined findings/diseases using a graphical interface. (d) The radiological test examination along with a typical ultrasound image from the hospital’s PACS in DICOM format.
MITIS: a WWW-based medical system for managing and processing medical images, as registered image (right image), from the application of the automatic boundary-based registration algorithm between the reference image (left image) and the unregistered image (centered image). Furthermore, the MITIS system allows the fusion of the reference and the registered image for further evaluation of a therapeutic scheme or the progression of a disease.
Table 5 Classification rates for normal and pathological categories of clinical data

<table>
<thead>
<tr>
<th>Normal cases</th>
<th>Pathological cases</th>
<th>Total cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification rate (%)</td>
<td>Classified subjects</td>
<td>Classification rate (%)</td>
</tr>
<tr>
<td>90.0</td>
<td>18/20</td>
<td>80.0</td>
</tr>
</tbody>
</table>

It must be pointed out that all mammographic images are imported in the MITIS system though the hospital’s PACS in DICOM format. In order to keep the network load as low as possible, even when dial-up connections are used (PSTN 56K, ISDN 64K), the images displayed on the screen can be compressed in JPEG format with varying dimensions (typically 512 × 512 pixels). Also, the system can export these images, except in DICOM format, in other formats including JPEG, TIFF, PNG, for further data manipulation with again varying dimensions.

4. Conclusions

In this paper a WWW-based medical system, called MITIS, has been developed for the management and processing of obstetrical, gynecological, and radiological medical data. The system, throughout its modular structure, records all the necessary medical information in terms of patient data, examinations, and operations and provides the user-expert with advanced image processing tools for the manipulation, processing and storage of ultrasound and mammographic images using the DICOM protocol. It can be installed in a hospital bringing together medical experts from different fields such as gynecologists and radiologists within the hospital as well as gynecological experts located outside of the hospital through the Internet.

The main functionalities offered by the MITIS system include:

- It records patient’s personal data, her children information data, the past medical history, the possible habits, allergies, drugs on use, etc.
- It monitors all possible patient’s examinations such obstetrical, gynecological, radiological at different times and places.
- It monitors the clinical situation of the mother and the fetus during pregnancy and schedules expected labor.
- It records all the laboratory data examination and the results of the breast clinical tests.
- It displays graphically the analysis of the measured hormones, weight, and systolic and diastolic arterial pressure during the pregnancy period.
- It offers advanced viewing capabilities based on computer graphics and image processing algorithms especially during the application of an operational scheme along with the findings/diseases.
- It incorporates a decision support system for the classification of specific regions within the mammographic images into two classes: normal and pathological.
- It includes manual and automatic schemes for the registration of mammographic images of the same patient for the evaluation of the progression of a disease or of a therapeutic methodology.
- The MITIS modular structure allows flexibility and expansion to include other gynecological applications. Also, the existence of predefined coded information within the MITIS system, results a very useful and simplified tool for monitoring any patient information inside and outside of a hospital.

Furthermore, the MITIS system was installed in the ‘Alexandra’ National Hospital, in Greece for the pilot study. Two departments within the hospital were able to successfully connect with the system; the gynecological and radiological departments sharing medical information. Since a number of private doctors are cooperated with the hospital, a number of five external gynecologists were successfully connected to the system. After a period of 5 months, where the system was under evaluation, more than 50 patients have been recorded and their examinations were successfully followed by the system.

Finally, the MITIS system is now fully operated and it is offered by the Infoproject S.A., a Greek software development company. More information about the system is available in the following address: http://www.infoproject.com.gr.

Acknowledgements

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References