Lecture Notes in Computer Science, LNCS 1345, December 1997, pp.4–17, Springer[a]

Medical Image Analysis and Simulation

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Abstract.
This article introduces the research field of digital image analysis and simulation applied to medicine.
Although the number of medical images produced in the world increases each year, their quantitative exploitation for diagnosis and therapy remains quite suboptimal.
This article reviews the potentialities offered by the research in digital image analysis and simulation, and presents a short survey of the state of the art.

1 Introduction

Millions of three-dimensional (3-D) and even four-dimensional (4-D) images of patients are produced every year all over the world to assess diagnosis and therapy. Most of them come from the following imaging modalities: Computed Tomography (CT), Magnetic Resonance (MR), Ultrasounds (US), and Nuclear Medicine (NM).

Medical images contain a lot of information on the internal geometry and on the functions of the human body. Unfortunately their current exploitation is usually purely qualitative. The observation is done in 2-D, on analogic supports (films), typically cross-section by cross-section, and one modality at a time.

Storing medical images in a digital format on the production site, and linking production sites together with high bandwidth networks has open a new era with the potential for a much more efficient and powerful exploitation of images.

We list in the next section the tremendous progress which could be made in the coming decade for a better and more reliable diagnosis and therapy of patients, with the help of automated medical image analysis and computer-assisted intervention.

Then we provide a list of current research issues in the field of medical image analysis, with pointers towards recent litterature before we conclude.

2 Improving Diagnosis and Therapy

2.1 Diagnosis

One of the major benefits of digital image analysis in terms of diagnosis is the introduction of **objective** and **quantitative 3-D measurements** in the images. These quantitative measurements cannot be extracted easily by hand from a succession of 2-D cross-sections. On the other hand, with adequate image processing tools, it should be possible to extract precisely the **size, location** and **texture** of specific **3-D anatomical** and **pathological structures**.

4-D images correspond to temporal sequences of moving organs, like the beating heart for instance. Here again, digital image analysis should provide a set of objective **motion parameters** to interpret quantitatively the motion, and establish quantified comparisons.

Even in terms of the *qualitative* evaluation of 3-D or 4-D images, digital image analysis should provide new modes of **visualization** more efficient than a purely 2-D static observation of chosen cross-sections. For instance one should aim at a realistic 3-D exploration on a powerful graphics workstation, both for static and dynamic organs, and from arbitrary dynamic viewpoints.

The presence of a network between connecting different production sites should allow to **fuse complementary multimodal images** together. For instance one should combine easily anatomical information from MR or CT images with functional information coming from NM images (SPECT or PET). Also, functional MR images could benefit from this type of image fusion.

Digital storage of medical images should also permit **temporal comparisons** between images taken at different times for the same patient, and automatically detect and measure any change.

Finally, digital image analysis should allow automatic **comparisons between patients**, as well as comparisons with a **digital anatomical atlas**. The objective could be either to retrieve similar anatomical structures or pathologies in large databases of medical images, or to detect significant differences with respect to "standard" anatomy.

2.2 Therapy

Once a diagnosis is established, medical images should again play an increasingly important role in the **preparation, control and validation of therapy**. This is true for most forms of therapy including radiotherapy, traditional surgery, video-surgery, interventional radiology, chimiotherapy...

In effect, the precise geometrical and physical information given by medical images should provide an accurate planning of care delivery. In most cases, **simulation** now appears as an intermediate stage between diagnosis and therapy itself. The idea is to build a model of a **virtual patient**, to simulate the result of the chosen therapy. Even more, medical gestures could be practiced in advance, either on a *standard* virtual patient on which it is possible to create as many artificial pathologies as desired, or on a virtual *template* of a real patient who must undergo a delicate intervention. **Surgery simulators** should become as common for surgeons as flight simulators for pilots.

During the intervention, **augmented reality** should allow pre-operative and per-operative images to be superimposed on the patient itself to provide useful additional information to the surgeon, typically the location of internal structures and/or pathologies. For instance the image of important vessels obtained from pre-operative MR angiography (MRA), could be superimposed on the video image of the patient, as if the patient was semi-transparent. Also per-operative 3-D Ultrasounds could allow the surgeon to "see" his endoscope, while navigating in delicate anatomical structures like brain, lungs, vertebra, etc...

Finally, it should be possible to **fuse images** taken **before** and **after therapy**, in order to assess quantitatively the differences.

3 State of the Art and Research Issues

Many of the problems addressed in the previous section are still open, and have generated an intense activity of research.

A good overview of the state of the art can be obtained from a selection of the chapters of the book *Computer Integrated Surgery* recently edited by Taylor, Lavallee, Burdea and Moesges [1], in a survey article by Pun, Gerig and Ratib [2], and in an article published by the author [3]. Also, the new participant to this field will be interested by a recent tutorial published by Acharya et al. [4] introducing the most popular biomedical imaging modalities currently in clinical use (CT, MR, Ultrasound, NM...).

In the sequel, and in order to present the state of the art in an organized manner, I tried to identify a set of "canonical" or "generic" scientific problems, which could be grouped under the terms **Segmentation, Visualisation, Registration, Morphometry and Atlases, Motion, Surgery Simulation** and **Medical Robotics**.

3.1 Segmentation

Segmentation is usually a first processing stage to extract regions or features of interest for another task (for instance visualisation, measurement, registration, motion analysis). There is no unique solution to this problem, but instead classes of tools (e.g. deformable models, scale-space analysis, mathematical morphology), which can often be combined together to reach a given goal. A general introduction to the topic was recently published in [5].

On the use of deformable models in medical image analysis, one should refer to the important survey written by McInerney and Terzopoulos [6], and the following references [7–9].

A lot of efforts are dedicated to scale-space analysis, as reports a recent tutorial written by B.M. Ter Haar Romeny [10]. This tutorial can be completed by articles on anisotropic diffusion in 3-D, [11–13]. Multiscale extraction of vessels is also an important topic discussed for instance in [14–16]. Cores are described by Pizer in [17].

Mathematical morphology is a powerful tool to segment images. Examples of its use with medical images can be found in [18]. Also, examples of segmentation techniques which combine image restoration, mathematical morphology and deformable models are given in [19].

MR images often require a bias field correction prior to any further processing. Recent publications on this topic are [20, 21]. One should also consult [22] on the segmentation of dynamic MR breast images using a model of contrast enhancement.

Differential features can be extracted in 3-D images to characterize edges, crest lines, ridges, and extremal points. These features are often used for registration purposes. Recent references include (but see also references in the registation section): [23–26]. A thorough analysis of multi-scale extraction of differential features in 3-D images was done by Fidrich [27].

Finally, extracting iso-surfaces in original or segmented images can be performed with the marching cubes algorithm [28]. Alternatively, and after an edge extraction is performed, this can be done with a Delaunay triangulation [29]. The marching line algorithm is powerful to extract lines defined at the intersection of 2 iso-surfaces, with subvoxel accuracy [30].

3.2 Visualisation

Historically, visualisation used to be the most active research field in 3-D image processing. G. Herman published a survey on the 3-D display of volumetric images [31], which can be completed by a less recent survey on the basic algorithms and systems for image rendering published by Stytz et al. [32].

In general, visualization requires a preliminary *segmentation* stage (previous section). A spectacular illustration of the state of the art in rendering possibilities is presented on the "visible man" data by Hoehne's team in [33].

3.3 Registration

Registration (or matching) can be performed intra- or inter-patients, between mono- or multi-modal 3-D images. This leads to rigid or non-rigid, mono- or multimodal registration algorithms. Also, some methods are feature based (using for instance the results of a segmentation), others use the raw intensity data.

A review of medical image registration methods with a classification was written by van den Elsen [34]. Also, an excellent survey of registration methods for computer integrated surgery was written by S. Lavallee [35]. Quite recently, a comparison of algorithms based on a retrospective evaluation was published by J. West [36]. Many references can be found in these 3 articles.

Among rigid registration algorithms, one can separate methods using geometrical features like ridges and/or extremal points [23, 24, 37, 38], and methods based on the minimization of a distance or correlation criterion: [39–44]. Recently, mutual information was introduced as a new measure to compare and register multimodal images: one can refer to the recent publications [45–47] and the references cited by these 2 articles.

The quantitative evaluation of the accuracy and robustness of rigid registration was studied by Pennec [48].

Finally, rigid registration can be computed between a 3-D image and a 2D projection including applications in virtual and augmented reality [41, 49–53].

Non-rigid registration is a much more difficult problem. Recent references on non-rigid registration include (but see also the morphometry section) feature based methods [54–57] and methods based on the raw intensity of the images [58–60].

3.4 Morphometry and Atlases

Morphometry consists in studying the geometry of shapes, and in particular the extraction of quantitative parameters, the computation of average shapes and the measurement of variations around them.

The definition of statistics on shapes requires a specific formalism, because they usually involve differential manifolds which are not vector-space (e.g. lines, frames, oriented points, rotations,...). The interested reader should refer to the excellent book by C. Small [61] which makes an excellent presentation of the pioneering work of Kendall and Bookstein, and to the work of X. Pennec [62, 63] who made significant extensions of the theory and experiments in 3-D.

Applications are related to the computation of quantitative anatomical atlases, and the analysis of inter-patient images. The references on these topics include the work of Thompson and Toga [64], A. Evans et al. [65], Bookstein[66], Dean et al. [67], Davatzikos et al. [68], Subsol et al.[69], Roberts et al. [70], Mangin et al. [71], Martin et al., [72, 73], Cootes et al. [74], Szekely et al. [75], Andreasen et al. [76].

A European project called Biomorph, funded by BIOMED-II, currently develops morphometric techniques for measurement of the size and shape of cerebral structures, with applications to multiple sclerosis and schizophrenia [77].

They are also related to the actual construction of anatomical atlases [78, 79] and also to indexation problems, in the sense that inter-patient comparisons can guide the selection of "similar" images in large databases of images [80].

3.5 Motion Analysis

Analyzing time series of 3-D medical images (i.e. 4-D images) is an important topic, especially for cardiac imaging. The objective is usually twofold: tracking the boundaries of some anatomical structure to estimate a displacement field, and quantifying the overall motion with a few objective and significant parameters.

On tracking, one can refer to the previously cited survey on deformable models [6], and also to feature-based methods, in particular methods using the curvature information along surface edges [81–84]. Some images have physical markers like in tagged MRI, or a local estimation of the velocity like in phase-contrast MRI. The physical principles of tagged MRI is well presented in [85]. Methods to recover the displacement of the tags are presented in [86, 87], and its extrapolation to the whole image is presented in [88, 89]. Methods adapted to phase-contrast MRI images are presented in [90, 91].

On the quantitative analysis of the motion field, one can refer to methods using a modal decomposition [92, 93], deformable parametric geometric models [94, 95], 4-D continuous deformation models [96], or other approaches [97–99].

3.6 Surgery Simulation

A lot of research has focused on spring-mass methods, because of their simplicity of implementation and their relatively low computational complexity [100, 101]. For example, [102] present a simulation of endoscopic surgery based on a surface spring-mass model. Although in this case the interactions are driven by instruments with sensors, no force feedback is used. The simulation environment at MERL [103] takes into account the volumetric nature of the organs with a deformation law derived from a spring-mass model. [104] have developed a model based on thin plates for endoscopic gall bladder surgery simulation.

Finite element models are less widely used due to the difficulty of their implementation and the large computing time. Nevertheless, [105] proposed a method for simulating features of the human eye with a complex behavior (large incompressible 3-D elastic deformations). Another example of eye surgery is given by [106], but still very far from real-time applications.

Reduction of computing time was studied by [107] using a condensation technique. With this method, the computation time required for the deformation of a volumetric model can be reduced to the computation time of a model only involving the surface nodes of the mesh. [108] described a technique for cutting linear elastic objects defined as finite element models. This technique was only applied to very simple two dimensional objects. One can also cite a method for free-form cutting in tomographic volume data [109] based on voxel operations for cutting and visualization.

In the Epidaure group at INRIA, we tried to integrate all the requirements for a realistic simulation. The static equations of the elastic model are solved by a modified finite element method which takes into account particular boundary conditions. The solution of these equations gives not only the deformed mesh but also the forces to be sent to a force feedback device according to the actual deformation. Finally, real-time interaction is possible thanks to a pre-processing of elementary deformations coupled with a speed-up algorithm. The linear elastic deformations, computed in real-time, give a first approximation of reality as reported in [110, 111]. This linear model was then improved to introduce non-linear biomechanical properties of soft tissues as reported in [112]. A good review of realistic soft tissue modeling in medical simulation can be found in [113].

3.7 Medical Robotics

Going from simulation to the actual performance of surgery or radiotherapy with a robot is also an active research area. For a flavor, the interested readers can consult the following recent publications involving robotics [114, 115], as well as a number of chapters of the book [50].

4 Conclusion

In this article, I tried to present the increasing role of digital image processing and simulation in medicine. I presented a list of potential improvements for diagnosis and therapy of the patient. I listed the major research issues attached to this field, and made a short survey of the current state of the art.

A striking aspect of this research field is the combined work of applied mathematicians, computer scientists, physicists and physicians, as well as the broad range of computer-science fields involved: image processing, computer-vision, graphics, and robotics.

These research efforts will bring a revolution in medicine in the future.

5 Acknowledgments

I have been helped in the preparation of this document by several persons including S. Cotin, J. Declerck, H. Delingette, G. Malandain, G. Subsol, and J.P. Thirion. I wish to thank them very much for their help, as well as the constant and stimulating support of G. Kahn.

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