Editorial

Advances in Biomedical Image Analysis

Past, Present and Future Challenges

T. M. Lehmann[1], **H. P. Meinzer**[2], **T. Tolxdorff**[3]
[1]Department of Medical Informatics, Aachen University of Technology (RWTH), Aachen, Germany
[2]Department of Medical and Biological Informatics, German Cancer Research Center (DKFZ), Heidelberg, Germany
[3]Institute for Medical Informatics, Biostatistics and Epidemiology, Charité – Universitätsmedizin Berlin,
Campus Benjamin Franklin, Berlin, Germany

Summary

Starting from raw data files coding eight bits of gray values per image pixel and identified with no more than eight characters to refer to the patient, the study, and technical parameters of the imaging modality, biomedical imaging has undergone manifold and rapid developments. Today, rather complex protocols such as Digital Imaging and Communications in Medicine (DICOM) are used to handle medical images. Most restrictions to image formation, visualization, storage and transfer have basically been solved and image interpretation now sets the focus of research. Currently, a method-driven modeling approach dominates the field of biomedical image processing, as algorithms for registration, segmentation, classification and measurements are developed on a methodological level. However, a further metamorphosis of paradigms has already started. The future of medical image processing is seen in task-oriented solutions integrated into diagnosis, intervention planning, therapy and follow-up studies. This alteration of paradigms is also reflected in the literature. As German activities are strongly tied to the international research, this change of paradigm is demonstrated by selected papers from the German annual workshop on medical image processing collected in this special issue.

Keywords

Computer-assisted image processing, computer-assisted image interpretation, automatic data processing, medical informatics applications, pattern recognition, three-dimensional imaging

Methods Inf Med 2004; 43: 308–14

1. Introduction

Biomedical image processing is an important and continuously growing field of research in medical informatics. Digital imaging modalities and the steady increase of computational power at decreasing costs enable sophisticated computer assistance in basic biomedical research, diagnosis, therapy, and control of patient treatment. In 1998, several German local activities were united by a joint workshop on algorithms, systems, and applications of medical image processing in Aachen. Since then, the workshop is held annually at different locations in Germany. The last meeting in 2004 took place in Berlin and was attended by more than 250 scientists from research, development, and application with contributions from Germany and several other countries. The papers, poster presentations and industrial showcases present novel techniques and applications from image acquisition, analysis, and understanding.

The continuous growth of German activities correlates with the international trends. For instance, the annual symposium on medical imaging, which is sponsored by the International Society for Optical Engineering (SPIE), rises both the number of oral and scientific poster presentations (Fig. 1) as well as the number of attendees. For instance in 1984, fewer than 25 papers were presented on image processing and analysis algorithms within the conference that was entitled “Application of Optical Instrumentation in Medicine” [6]. By 1994 and 2004, there were 88 and 232 papers in the conference track “Image Processing” that has been established in 1989, resulting in a large extention to this track among the other conference tracks (Fig. 1). In addition, a substantial part of the other tracks is also about image processing technologies or algorithms. The same tendency is observed for the International Symposium on Biomedical Imaging (ISBI), which was founded in 2002 by the Institute of Electrical and Electronics Engineers (IEEE). However, those figures do not answer the question which major progress has been made in the field of biomedical image analysis and which challenges still need to be addressed in future work.

Duncan and Ayache have recently described the progress of medical image analysis over two decades [3]. They termed pre-1980 to 1984 the era of two-dimensional (2D) image analysis, 1985-1991, when knowledge-based strategies came to the forefront, 1992-1998, when the analysis of fully three-dimensional (3D) images became the key goal, and 1999 and beyond, when advanced imaging and computing technology facilitate work in image-guided procedures and more realistic visualization. But what exactly is meant by advanced imaging and computing technology? According to Talmon and Hasman, medical informatics is, in general, a modeling discipline that aims at designing models for medical processes in order to implement them in computer systems [13]. Making these models applicable for daily medical practice is the applied science or engineering side of medical informatics. Hasman et al. have categorized these processes into biological, communication, decision, engineering, educational, organizational, and computational processes [7]. Obviously, biomedical image analysis mainly addresses biological processes, decision making, and computational aspects. From this point of view, it is important whether one can identify the particular processes behind advanced biomedical imaging.

In this paper, we will try to term such processes that are assisted by applying medical image processing techniques. We will scrutinize the past and present of image processing and analysis with respect to any alterations of the paradigms underlying the modeling process of medical imaging informatics. Based on this appraisal, we will predict future directions of biomedical image processing, where the papers contained in this special issue are dedicated to exemplarily emphasize current research and future developments in the broad field of medical imaging informatics.

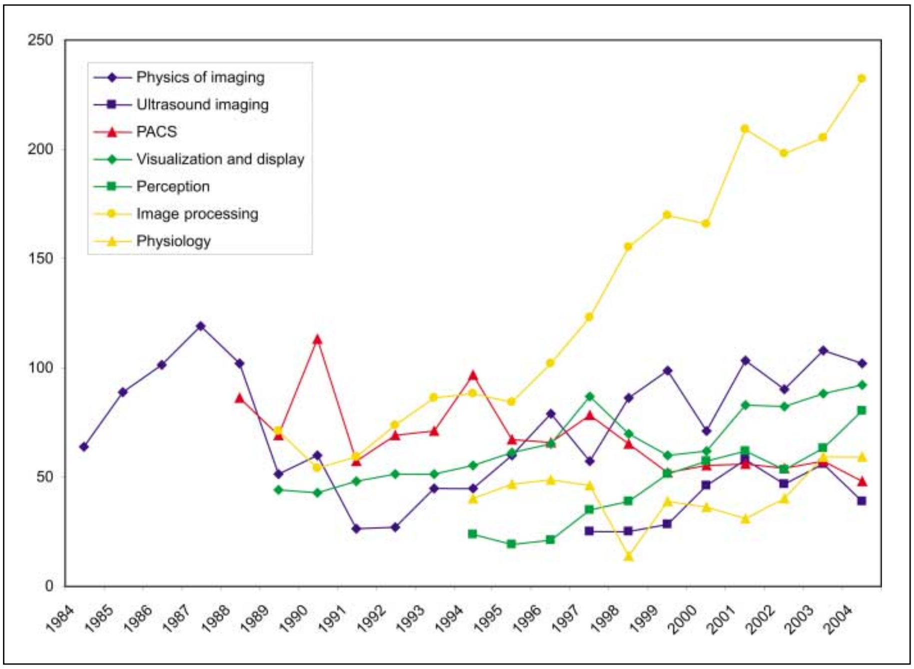

Fig. 1 Number of presentations at SPIE's Medical Imaging according to the conference tracks. The colors are selected to denote the relations between the symposium tracks.

2. Past – Image Acquisition, Display, and Management

In the following, we will draw a scenario that could have been at any institution pioneering biomedical image processing. In the early years of research, image generation and handling was extremely difficult, since the computers were of less than a thousandth of today's computing and storage capacity. Therefore, reading out the data from the imaging device and computing a medical image that displays valuable information was a major challenge. Consequently, algorithmic improvements addressed the speed rather than the quality or accuracy of processing.

2.1 Image Formation (Digital)

In the beginning, there was a raw data file carrying a name which was not allowed to be composed of more than eight characters and thus degenerated to a cryptic abbreviation concocted from a patient's identification, an examination identifier, a slice number and all other pertinent information. It consisted of an unformatted bit-stream that had to be deciphered. If the decoding did not result in at least a halfway decent morphological structure as compared to those displayed in the anatomic textbook, attempts were continued with the same suspense that arises when decoding a secret service message. The books of Pratt [11], Gonzales and Wintz [4], which has later turned to Gonzales and Woods [5], as well as the publications of Rosenfeld and Kak [12] were piled up between the terminal's keyboard and the impulse-dialing telephone, while one pondered whether the data to be processed had its origin at the top or bottom left or whether it consisted of an eight or twelve-bit depth. If necessary, a phone call was made to check, but this effort was doomed to failure with most of the modality producers or vendors. When this problem was solved, the look-up tables were programmed manually. Prominent problems were raised from simple questions such as how to segment 256 codes into color and gray values or which role should color play: Should it refer to the function of tissue or should it clarify morphological information?

2.2 Print and Display

The one and only mainframe of the clinical center was extended by some exotic hardware: A loud roaring cabinet now stood in the computer room, and each delegation passing by was given the proud explanation: this is a digital image server with the enormous capacity of one megabyte. It can even handle color images, which can be viewed only on a television monitor that – due to the noise – was placed in a separated room and connected by four coaxial cables.

The system halted regularly about every 30 minutes, which required a manual reset by the operator to continue image processing. Only if one succeeded in distracting the operator's attention, the images could be printed out. With the help of the magical symbol "1H+", the line feed of the typewriter printer was temporarily deactivated and gray values were simulated by skillfully printing characters on top of each other. Frequently, the operators had become alerted to this acoustic abnormality and stopped the printing process before the continuous paper was cut off.

2.3 Pixel Data Manipulation

Those were the days when each image manipulation had to be painstakingly programmed beforehand. The rank growth of minor private subroutine libraries sprouted tremendously. Laplace operators, Hough transformers, Prewitt operators were developed with a great deal of effort and then personally tested with as much effort and diligence. A Fourier transform took so long that it left you time enough to slowly work your way through the next chapter of Gonzales and Wintz before having to face the results of your art of programming. It was an enormous improvement when one of the first parser generators appeared on the scene – a generator which allowed a comfortable, command-orientated control of image-processing libraries. It is now hard to imagine working with processing power of less than one megahertz or even with non-quadratic pixels.

2.4 Storage and Transfer

In these early years, standards were non-existent [9]. This word was not only "not mentioned", it was unknown and unexplored. The first experiments with databases were made, since the cryptic abbreviations of patients' names caused enormous problems in relocating entire series of images – even on a hard disk on only 10 MB of capacity. Of course, there was no integration of other systems like hospital information systems (HIS). Although radiological information systems (RIS) and picture archiving and communication systems (PACS) were already postulated, their endless development had not yet begun.

If images were needed for publications, the light in the lab was turned off, and the monitor was photographed with a camera and tripod. When a paper was finally finished, the color prints were stuck in manually. Also, the paper had to be mailed at least ten days before the deadline in order to arrive in the United States on time.

2.5 Acceleration

If you would have asked the physician when he would like to receive his image via the electronic network at his workstation, he probably would have answered: within one or two days would be great. However, this faced remarkable problems to the computer scientist, since he was required to stray through long corridors at night in order to press a reset button just to be able to work undisturbed again for a couple of minutes. Fortunately, these days have passed and the underlying infrastructure-oriented paradigms of image formation, pixel data manipulation, visualization, storage, and transfer have basically been dissolved. Today, the answer of the physician will be: one or two seconds, which is possible for many algorithms and procedures using modern hard- and software.

3. Present – Image Analysis

In the mid-eighties, a first change in the paradigms of medical image processing was notable [3, 6]. Digital generation and handling of medical imagery was extended to image analysis. Therefore, a priori knowledge had to be integrated into the algorithms that were designed for medical image processing. Consequently, the processes modeled by medical imaging informatics transformed from a structure-driven into a process-driven scheme (Fig. 2). According to Hanson, the acceptance of computed tomography (CT) led to the question: Are there other ways in which computers could help radiologists interpret medical images? [6]. With respect to the SPIE's International Symposium on Medical Imaging, the track "Image Processing" was established in 1989 to answer this question. Exemplifying prominent categories in this track, deformable models are mentioned that have become prevalent in many areas of image analysis. Note that such a method-centered view reflects the process-driven paradigm presently being dominant in medical image procession.

This process-driven scheme is of technical nature. It follows a stepwise sequence of image data transforms rather than a patient-centered application of image analysis. Still, image formation is the first module of this technical processing scheme, which is followed by registration of pixel data, segmentation and classification of relevant objects, as well as quantitative measurements in order to obtain additional information supporting the physicians decision of diagnostics or intervention planning (Fig. 2). Up to now, this view on medical imaging informatics is most prominent and the majority of recently published papers fits into the scheme.

3.1 Image Formation (Functional)

Since the goal of today's image analysis is image interpretation and quantitative measurements, functional imaging has become the key challenge of biomedical image formation. Functional magnetic resonance imaging (fMRI) is the most popular example. However, MRI palpation or ECC-triggered MRI volumetry of the beating heart are further examples. In general, today's technology optimizes the resolution of established techniques or adds dimensionality. As postulated by Duncan and Ayache, fully 3D images are currently the goal [3]. Consequently, novel techniques such as tuned aperture computed tomography (TACT®) or limited angle tomography reconstruct 3D volumes from an incomplete number of projections [Linnenbrügger et al.: Automated Hybrid TACT® Volume Reconstructions; Weber et al.: A Linear Programming Approach to Limited Angle 3D Reconstruction from DSA Projection (this issue)]. The knowledge required for the reconstruction process is obtained from other modalities, e.g., photography in hybrid TACT, or application-specific assumptions, i.e. modeling the imaging process with certain respect to the context of the images.

3.2 Registration

Frequently, one cannot combine different modalities prior to image acquisition and formation. Nonetheless, improvement of measurement accuracy or resolution is obtained from multimodal combinations. Consequently, registration of pixel data is a key module in many image processing techniques in medicine [Fischer and Modersitzki: Intensity-based Image Registration with a Guaranteed One-to-one Point

Match (this issue)]. Unimodal registration is required for follow-up studies and the reliable detection of tissue alterations. Multimodal registration enables the transformation of the high resolution of morphological imaging to functional images, which are usually acquired with significant lower resolution. Especially in neuroimaging, digital atlas processing is based on powerful and robust registration techniques. It enables the transfer of a priori knowledge on important brain areas onto the structure of a certain patient's brain, which might significantly differ in morphology.

3.3 Segmentation

With respect to the process-driven paradigm of current image processing in medicine, segmentation is the most essential part of the processing pipeline. Segmentation means localization and delineation of relevant structures such as important objects. While humans can usually perform the localization part of image segmentation superior to computer algorithms, the delineation part is the typical domain of biomedical image processing and analysis. Computer-based segmentation yields detailed and reproducible shapes and/or surfaces of relevant objects [Bartz et al.: Accurate Volumetric Measurements of Anatomical Cavities (this issue)]. Again, a considerable amount of a priori knowledge is modeled on a rather high level of abstraction. Consequently, automatic segmentation algorithms are specialized to a certain application such as the optical disk in retinal images [Chrástek et al.: Multimodal Retinal Image Registration for Optic Disk Segmentation (this issue)] or overlapping cells in digital microscopies [Wittenberg et al.: A Semantic Approach to Segmentation of Overlapping Objects (this issue)]. They are inapplicable to other objects of interest or other imaging modalities without redesigning the procedure, because an adequate formulation of a priori knowledge on the new content is required.

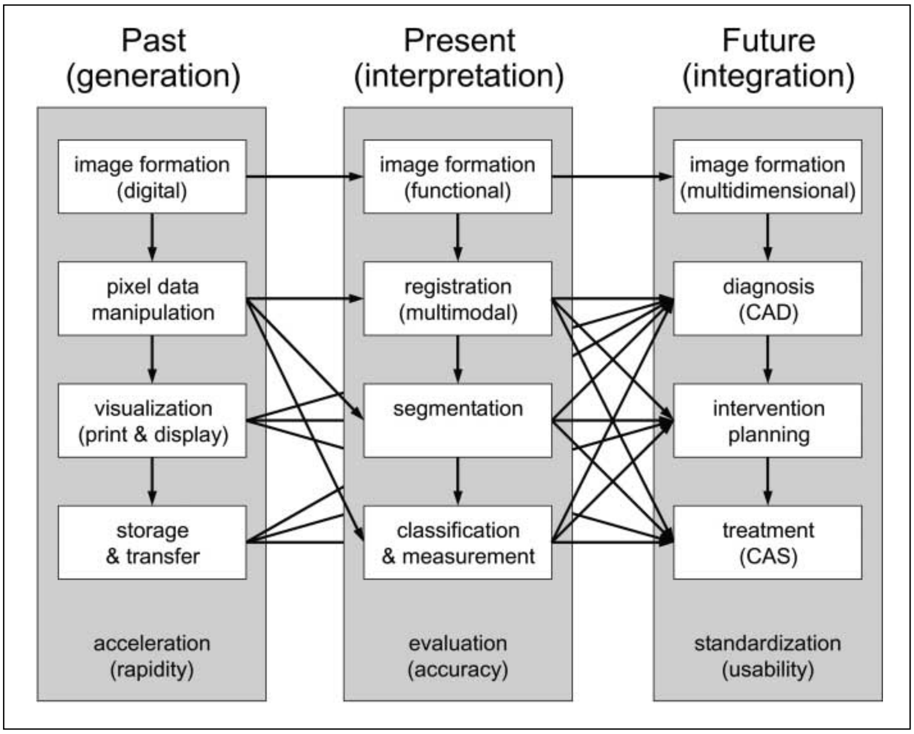

Fig. 2 The paradigms of medical image processing during the past, at present, and in the future

3.4 Classification and Measurement

Once the relevant objects have been identified within the image, image analysis aims at providing quantitative measurements to the physicians. According to the processing scheme that models the technical steps, features are extracted from the segments in order to classify them. Usually, these features reflect the biomedical application. However, the increasing amount of routinely acquired digital images opens a novel field of research, where a general classification of images is the central focus. In particular, content-based image retrieval in medical applications requires automatic classification of pixel data with respect to the imaging modality and technical parameters used, the relative orientation of the imaging device and the patient, the body region examined, and the biomedical system under investigations [Lehmann et al.: Content-based Image Retrieval in Medical Applications (this issue)]. Here, the context is unknown prospectively and must be determined automatically in order to optimize successive modules of the image processing pipeline.

3.5 Evaluation

Although enormous efforts in biomedical image processing have been made during the last 15 years, sophisticated algorithms for registration, segmentation, classification, and measurement are infrequently applied in daily routine of health care. Obviously, there are two reasons. Firstly, the process-driven scheme mismatches a patient-centered application. This fact is already acknowledged since science and technology currently changes the general paradigm of modeling image processing (see next section). Secondly, the algorithms simply fail when applied in clinical routine since the data acquired routinely differs from those references that were available during development. Some assumptions that are inherently used by the algorithms do not hold for routine data. In other words, the algorithms have not been sufficiently evaluated for routine use. Consequently, systematic evaluation of medical image processing techniques is in the focus of current research [Krüger et al.: Evaluation of Computer-assisted Image

Enhancement in Minimal Invasive Endoscopic Surgery; Uhlemann et al.: Objective Evaluation of Three-dimensional Image Registration Algorithms. Tools for Optimization and Evaluation (this issue)].

Over a period of 20 years, the belief in image processing was that if a result computed on the *Lena Image* is improved, the novel algorithm is generally superior to existing processing schemes. We know today that a sufficient number of reference data is required for exhaustive evaluation and statistical analyses need to be applied. We also have learned that the ground truth plays an important role for reliable evaluation and that manual references such as object outlines drawn by a medical expert are itself unreliable and, therefore, inapplicable for reliable evaluation. Consequently, the generation of valid references and ground truth is covered by current research [Uhlemann et al.: Objective Evaluation of Three-dimensional Image Registration Algorithms – Tools for Optimization and Evaluation (this issue)].

4. Future – Routine Application

Up to now, the process-driven view on medical imaging informatics is dominant and the majority of recently published papers match this scheme. Nonetheless, a second metamorphosis of paradigms already began a few years ago. In the future, the patient will be at the center of biomedical image processing and novel algorithms are primarily designed to fit into routine application. Integration and routine use are major challenges of further developments in a result-driven view of biomedical image analysis [1].

Therefore, medical imaging will increase its impact in the next decade, but it will become less apparent than it is now. Classic radiology still deals with 2D film images. The end of these times already has come as the new multi-slice CTs are making much too many images per patient to be printed and analyzed in the old fashion way. Therefore, new challenges arise from handling and processing the increased data volume. Also, all effort of the medical imaging community will be in vain if our support is not fully integrated into the clinical workflow. The medical users are not interested in technical problems and procedures. They demand help in diagnoses and therapy planning. Only systems that increase productivity and safety while reducing costs will be accepted. Everything must be easily accessible, requiring no training time and being used by intuition. This result-driven approach forms the underlying paradigm of future image analysis (Fig. 2).

4.1 Image Formation (Multidimensional)

Continuous image formation is an essential part of this new paradigm. The times of 2D images are over. The availability of serial multi-slice data represents de facto volume data (3D) and if taken at a number of times, four-dimensional (4D) data is obtained. Perhaps it is clearer to refer to these data as 3D-plus-time data (3D+t). Either the space changes over time, e.g. if a patient is scanned several times for follow-up controls, or the object in the space is moving, e.g. a beating heart or a moving diaphragm due to breathing.

The availability of these 3D and 3D+t data will change the focus in medical imaging from 2D image processing to 3D and 4D image processing [König and Hesser: Livewires Using Path-graphs (this issue)]. Parallel to this we will observe an increasing resolution in space and time. This will permit us to present ever increasing details which will improve even more the relevance of image guided diagnostics and therapy.

4.2 Diagnosis

The old and well known software algorithms will be extended to the additional dimension. This will demand higher computational power and more memory. The development of the hardware is so fast that we do not foresee upcoming shortcomings. The hope of the past that there will be some kind of automated understanding (i.e. diagnoses) collapsed due to our failing understanding of human perception in general. Thus, there will be some 'intelligent' semi-automatic (i.e. interactive) procedures, including the medical doctors, who by this will keep their responsibility and control of the process [Hahn et al.: A Reliable and Efficient Method for Cerebral Ventricular Volumetry in Pediatric Neuroimaging; Wagenknecht et al.: MRI-based Individual 3D Region-of-interest Atlases of the Human Brain. A New Method for Analyzing Functional Data (this issue)]. For instance in traumatology, there will be devices that can show 3D/3D+t representations of a patient within minutes after the patient left a fast spiral multi-slice CT, putting all interesting features to the fingertips of the medical doctors (e.g. F1 is skeleton, F2 is respiratory system, etc.)

4.3 Intervention Planning

Although remarkable efforts have already been made, the development of detailed atlases and powerful mapping tools are still needed to allow one to locate morphological landmarks or functional areas in individual patient data are still needed. Computer-assisted intervention planning will be based on those meta-data in many medical fields. In future, atlases will not only be focused on hard tissue to assist orthopedic surgery [Ehrhardt et al.: Atlas-based Recognition of Anatomical Structures and Landmarks and the Automatic Computation of Orthopedic Parameters (this issue)] but also on soft tissues such as the brain or other organs. Furthermore, powerful visualization will strengthen the planning of micro-invasive surgery [Weichert et al.: Registration of Biplane Angiography and Intravascular Ultrasound for 3D Vessel Reconstruction (this issue)].

4.4 Therapy

The logical next step in the developmental process is the extension from diagnostic support and therapy planning to the support of therapy. One example is the control of 'smart' handheld instruments for cutting, drilling, ablation etc. [Vogt et al.: Light

Fields for Minimal Invasive Surgery Using an Endoscope Positioning Robot (this issue)]. Since this will be possible by the knowledge of the topology and surgical practice in general, the key word is navigation. We do not believe in a wider use of robotics in surgery. Smart instruments in the hands of a physician, such as navigated endoscopes promise access to most internal locations with minimal collateral damage to the patient. Once inside, the physician can cut, heat, cool, radiate, whatever is indicated.

4.5 Standardization

As mentioned before, we need valuable standards to replace the de facto standards such as the *Lena Image* for evaluation. As a joint German, European and American initiative, annotated data collections are currently being established for exhaustive evaluation of medical image processing and will assist future algorithmic developments [Horsch et al.: Establishing an International Reference Image Database for Research and Development in Medical Image Processing (this issue)].

Another field of cooperative impact is the information technology (IT) in a hospital. We foresee integrated clinical access to all relevant patient data, integrating HIS, RIS, PACS, the clinical chemical laboratory data, pathological images and so on. The old disjunctive islands of IT in health services will be overcome. For this we need standards and the integration of standards. The DICOM standard will expand into other fields by adding features for e.g. radiotherapy (DICOM-RT) and structured reporting (DICOM-SR). The strongest impact on clinical integration will come from the Integrating the Healthcare Enterprise (IHE) consortium. All data are available wherever and whenever needed (ubiquity). The standards for the biomedical imaging community will e.g. be the Imaging Toolkit (ITK), the Visualization Toolkit (VTK) and the Medical Imaging Interaction Toolkit (MITK). The dependence of operating systems will be reduced, e.g. by application programming interfaces like Qt® of Trolltech®, Oslo, Norway, that compiles into any operating system. Furthermore, systems with proprietary software will disappear.

The integration of IT in health care will not stop inside of hospitals. There will be regional and global collaboration. Groups of local health care suppliers will cooperate to provide the best possible care by reduced costs, sharing resources. All kinds of services will be collaborating, including high-end facilities like university hospitals and rehabilitation centers. The competence for the preparation and correct interpretation of the new 3D and 3D+t images will probably not be available in all locations. Centers of excellence will supply support of specialists, dedicated to special complex problems. This will be based on integrated networks, based on IT-technologies. Images will play a central and vital role in these networks, because “an image tells more than 1000 words”.

5. Discussion

In this paper, we have analyzed the paradigms underlying the modeling process of biomedical imaging informatics. Two major metamorphoses have been identified. The first was manifested in the beginning of the 1990ies, when the goal of image processing was termed interpretation and understanding for automatic analysis and measurements. This observation is in agreement with Duncan and Ayache [3] and also reflected by international activities such as the SPIE’s International Symposium on Medical Imaging. In 1989, when the symposium was already titled “Medical Imaging” and consisted of two conference tracks, one called “Image Formation, Detection, Processing, and Interpretation” and the other “Image Data Management and Display”, a third conference track “Image Processing” was established as an independent track (Fig. 1). It is also interesting to note that the conference track on PACS is slowly but steadily decreasing. This manifests our statement, that former significant problems to handle the biomedical imagery is now basically dissolved.

The second transform of paradigms leads from the process-oriented scheme to an application-oriented model. Again, this thesis is reflected in the history of SPIE (Fig. 1). In the mid 1990ies, conference tracks such as “Physiology, Function, and Structure from Medical Images” or “Image Perception, Observer Performance, and Technology Assessment” were born. Here, the usability of biomedical imaging informatics is at the center of algorithmic developments. In accordance, Kulikowski et al. claimed the integration of results from automatic image segmentation as a major challenge of imaging informatics [10]. Haux has recently defined the role of medical informatics for health care in the information society [8]. The major aims that still have to be achieved are the 1) patient-centered use of medical data, 2) process-integrated decision support, and 3) comprehensive use of medical data.

6. Conclusion

In summary, the past, present, and future of biomedical image analysis reflects the paradigm of quality management, where structure, process, and result quality are distinguished [2]. While most of infrastructure- and processing-pipeline-related problems have been already resolved, the future of biomedical image processing lies in the results obtained from our methods. These results will be measured in terms of the direct benefit to the patient. Consequently, medical image processing is worthless unless applied routinely and integration of robust image processing is the next major challenge to face.

Acknowledgment
The authors would like to thank Ken Hanson, Los Alamos National Laboratory, Los Alamos, NM, USA for providing detailed data of the history of SPIE’s International Symposium on Medical Imaging.

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Correspondence to:
Thomas M. Lehmann
RWTH Aachen
Institut für Medizinische Informatik
52027 Aachen
Germany
E-mail: lehmann@computer.org