COVIRA: C0mputer VIision in RAdiology

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ABSTRACT. This paper presents the main results achieved by the COVIRA consortium project during a 15-months period under the AIM Exploratory Action programme. The prime result of the project is a specification of a system for knowledge based interpretation of cranial MR images as a means of computer assistance in diagnostic radiology, radiation therapy planning and stereotactic neurosurgery. This specification is based on demonstrated results from prototypical implementations and an analysis of the state-of-the-art and of the clinical requirements.

Image segmentation and interpretation results were obtained for a set of test images of tumor patients selected by medical experts from the above fields. For each patient slice, two MR spin echo images are available.

For image segmentation, results are presented for three schemes: one using a Canny edge detector followed by a smooth patch fitting for region finding, another using a region detection according to Nagao/Matsuayama and a Marr-Hildreth edge detector based on one of the echoes to guide region merging, and a third scheme using a multiscale approach to edge detection.

The image interpretation results presented are based on a case model representation of clinical, anatomical, MR-Physics, and tissue parameter knowledge. Results are presented for two schemes: one using a fuzzy clustering approach providing a fuzzy segmentation and a subsequent fuzzy relational matching step, and another using a blackboard approach based on the classical low-, middle- and high-level of processing, allowing for a dynamic control with feedback and backtracking mechanisms.

The results were comparatively evaluated by medical experts based on criteria of clinical usefulness.

1. Introduction

The COVIRA project addressed the area of knowledge based interpretation of cranial Magnetic Resonance MR images. The prime goal of the project was to make hard- and software specifications for a system

- for knowledge based interpretation of cranial MR images,
- suitable for applications in diagnostic radiology, stereotactic neurosurgery and radiation therapy planning, and
- based on demonstrated results from prototypical implementations and an analysis of clinical requirements.

The main action lines in the project were

- to analyze the state-of-the-art of computer assistance in the above mentioned areas of clinical neurosciences,
- to provide requirements for future computer assistance tools in these areas,
- to produce a computer representation of the relevant medical and sensor-specific knowledge,
- to produce a prototypical implementation of several approaches to image segmentation,
– to produce a prototypical implementation of two approaches to image interpretation,
– to perform a comparative evaluation of the results by the involved clinicians.

In this paper, we report on the results achieved for these action lines by the clinical partner, the two clinical subcontractors and the four technical partners in the COVIRA consortium [1].


A survey of the state-of-the-art and an analysis of the clinical requirements for computer assistance in the clinical neurosciences was carried out with the clinical partner and the subcontractors from the three clinical disciplines mentioned above. The current status of computer assistance suffers from deficiencies of tools for quantitative analysis in diagnostic radiology together with a lack of PACS environment. In radiation therapy planning and stereotactic neurosurgery, the current support lacks suitable processing speed, adequate tools for 2D and 3D segmentation in general, efficient interaction (especially in 3D) and adequate 3D display functionality.

In terms of requirements, tumor detection and characterization based on lesion shape, density, invasiveness and effect on normal brain structure are most important in diagnosis. Accuracy in 2D image segmentation, achieved quickly and with a minimum of user interaction, is a prerequisite for reliable tools for any clinical use. For therapy planning and stereotactic neurosurgery, tumor localization based on target coordinates and 3D image correlation methods are required allowing to combine CT, MR and angiographic information. For reliability reasons, information must be transferred from MR and angiographic images onto CT images, the latter being geometrically more accurate and indispensable for radiation treatment planning. Intrinsic uncertainty must be dealt with in a suitable manner. User interaction and 2D/3D display must be optimized for efficiency. Since in neurosurgery computation is done during the operative intervention, very fast processing is required and the user interface should be optimally adapted to the clinical tasks.

If successful, clinical use of computer tools will achieve better supported diagnosis, safer and more successful treatment, reduction of traumatic side-effects of therapeutic interventions and reduction in hospitalization time and cost.

3. Specification and Implementation of Knowledge Representation Schemes

In the COVIRA project, the symbolic processing is related to a 'case model' for the representation of the knowledge relevant to a particular medical case. The case model thus is a standardized, portable representation of knowledge which allowed different interpretation approaches to be comparatively evaluated based on identical pictorial (two echoes for each MR scan) and model input data.

The case model representation was specified and realized as a propositional data structure in the form of a semantic network. It consists of a subset of entries (relations) in four knowledge sources that are relevant for the medical case under consideration. The structure of the case model and a common file format for exchanging actual models between partners were jointly defined. The four different knowledge sources are:

The Clinical Knowledge Source was structured and specified on the basis of the 'Parisian Nomina Anatomica' (PNA), and contains a classification of brain tumors according to the WHO standard. The clinical knowledge source allows to generate lesion localization hypotheses from clinical data in patient dossiers.

For the Anatomical Knowledge Source, a hierarchy of anatomical units with part-of relations and a set of attributes and further relations was defined and implemented as a semantic network. The current implementation contains only 2D information, but the representation scheme is suited for 3D also. The anatomical knowledge source guides the image interpretation process by providing hypotheses about anatomical object structure, location, adjacency and shape.
The MR Physics Knowledge Source represents a model providing all relevant information about the MR scanning device and physics.

The Statistical Knowledge Source provides a translation of anatomical terms into histological tissue types, for which the MR tissue parameter statistics were represented from an extensive literature survey on measured T1 and T2 relaxation times and proton density.

From the MR physics knowledge source and the statistical knowledge source, hypotheses can be generated about the signal intensity of anatomical objects in the measured image and contrast relationships for pairs of objects. They also provide information about the noise in the image.

4. Image Segmentation Approaches Followed in COVIRA

Segmentation is an important first step in analysing an image. A segmented image represents the information in the image by delineating the boundaries between image regions which correspond to different objects. This allows the volume of information to be reduced, and provides a description of the image content more adapted to image analysis.

In COVIRA, two partners investigated two principal methods of image segmentation which are based on combining edge and region information. Another partner has investigated a multiresolution segmentation scheme to derive descriptions of image structure in the discrete noisy intensity functions of MR images.

4.1 Edge/Region based image segmentation

Edges correspond to local discontinuities in the grey level function of the image. These local discontinuities characterise the abrupt intensity variations that often indicate the presence of an object in the image and can thus be used for image segmentation. Many techniques for edge detection were reported in literature.

Another approach to image segmentation marks homogeneous regions in the image, i.e. the image is described by segmenting it into sets of points that possess certain properties of homogeneity. For example, smooth regions can be detected on the basis of their roughly constant or perhaps smoothly varying intensity, whilst textured regions can be detected on the basis of the similarity of the texture across them.

From a theoretical point of view, the two approaches are complementary, in the sense that knowledge of the edges allows the regions to be deduced and vice-versa. However, in practice the two methods give rise to different algorithms that produce different results, each having its own peculiarities. It is possible to allow the two techniques to cooperate, rather than just choosing one of them. However, there is as yet no definitive method for combining edge and region information to improve the segmentation. Thus, there are two possibilities, i.e. to give priority to the edge information (done by partner P1) or to give priority to the region information (done by partner P2).

4.2 Image Segmentation Starting with Edge Detection (Partner P1)

Partner P1 (IBM UKSC [1]) chose to take the edge information first, and then used a region growing algorithm for the detection of smooth regions to provide information that can be used to fill in the discontinuities in the edge map. By integrating the two methods in this fashion, better segmentation results were expected. The aim of this approach was to achieve the best possible segmentation without domain-specific knowledge.

The edge detector is that of Canny [2], which is one of the most successful. It has some deficiency, notably in the area around junctions. However, this deficiency was rectified, using the method of Li, Sullivan and Baker [3]. One of the major advantages of using Canny in this application is that it gives clean edges with good localisation. This is coupled with a state-of-the-art region growing algorithm, similar to that of Silverman and Cooper [4], which fits smooth constant or quadratic patches to the regions. The edge information is obtained from an image which is the average derived from two input images (first and second echo) and subsequently used to generate seed points for the region grower. The algorithm also limits the growth of the regions, thus intimately linking the two processes. For further details of the algorithms, see Brelstaff, Ibison and Elliott [5].
Fig. COVIRA-1: Original MR image (left) with overlaid computer segmentation result from P₁ (right), case 1451/9.

Fig. COVIRA-2: Original image and segmentation result from P₁ for another clinical case, case c2065/7.2.

Fig. COVIRA-3: Original 1st and 2nd echo images (left), computer segmentation (green on the right), manual segmentation (yellow on the right), and manual contours identified with the computer to within ±1 pixel (red in center).
Fig. COVIRA-1 shows a typical MR image on the left, with the computer segmentation overlaid on the right. The Canny edges are shown in green. It will be noted that there are a number of gaps in these edges which were completed by the region grower (shown in yellow).

Fig. COVIRA-2 shows the result for another MR image. The clinical usefulness of the segmentation in fig. COVIRA-1 was evaluated by comparing it to a manual segmentation performed by radiologists at partner P5 (CAM, G. Maranon General Hospital Madrid [1]). The tool for manual segmentation is described below. 84% of the boundaries chosen by the clinicians were identified, within one pixel, by the computer segmentation. This is shown in fig. COVIRA-3. On the left are the original images (first and second echo). On the right are the computer segmentation (in green) and the manual segmentation (in yellow). In the centre is the manual segmentation with the boundaries identified by the computer shown in red (unidentified boundaries in yellow).

4.3 Image Segmentation Starting with Region Detection (Partner P2)

At Partner P2 (DIBE, Univ. of Genova [1]), the basic idea was to initially divide an image into a large set of small regions by applying a fast pre-segmentation algorithm grouping only very similar pixels. As an example, the contours of the pre-segmentation regions extracted from the two MR echoes shown in the upper portion of fig. COVIRA-4 are displayed in the lower left portion of the same figure.

The final regions into which the image is segmented are obtained from these small regions by successive merging steps which take into account similarity of geometrical and densitometric region features as well as the edges obtained from an edge detection algorithm based on the Marr-Hildreth approach [6]. An example of this approach applied to the second echo of an MR image is shown in the lower right portion of fig. COVIRA-4.

The final result of the segmentation after region merging is a set of regions, the boundaries of which are displayed in fig. COVIRA-5 as an overlay on top of the original second echo MR image. The respective contours are thus always closed as opposed to those obtained with the approach of P1 (UKSC).
4.4 Multiresolution Approach to Image Segmentation (Partner P3)

The multiresolution approach to segmentation followed by partner P3 (Univ. of Hamburg, [1]) aimed at the derivation of local exhaustive descriptions of image structures in discrete noisy MR and CT intensity functions. Particularly the numerical determination of an image description which represents a causal relationship between image structure and patient morphology was addressed. The major objective of this approach is an extensive analysis of what can be achieved with theoretically derived and inherently parallel bottom-up methods before deciding upon

- the nature of further computational processes as well as
- introducing either certain levels of interaction or domain-specific knowledge.

Here image structure is understood to be, apart from junctions or regions, mainly ramp edges with gradually changing local contrast (which are in particular prominent in CT and MR images due to the partial volume phenomenon in slices with anisotropic spatial resolution) and smooth contours. The developed methodology implies discrete convolution operators at different scales, scale-space integration of operator responses, and a standard Gaussian model of isotropic white noise [7]. Numerical results are given in the form of a set of intrinsic images each of which represents location and polarity of edge points, local contrast, local width of smooth contrast transitions (e.g. tissue-ventricle borders), greylevel gradient vector and tangent fields (see Figs. COVIRA-6 to COVIRA-8). Experiments with the first discrete implementation of the multiresolution theory clearly exhibited the capability to reliably and accurately estimate intrinsic local characteristics of the image intensity function by a pure bottom-up scheme characterized by a significant degree of inherent parallelism. In a complementary way, a theoretical investigation into the principal error bounds of edge point localization schemes was undertaken considering computational vision processes as a quantitative mensuration tool, e.g. a calibrated instrument for medical domain applications [8].

Fig. COVIRA-6: Case 1451 1st echo: Integration edge map after 10 scales. Scale space (0.5; 0.6; 0.7; 0.8; 0.9; 1.0; 1.25; 1.5; 1.75; 2.0). Thresholds for hysteresis: TU = 21, TL = 7.

Fig. COVIRA-7: Intrinsic polarity: visual representation. Black indicates positive contrast, white indicates negative contrast from right to left.
4.5 Image Segmentation Based on Iconic Fuzzy Sets (Partner P4)

The approach pursued by P4 (Philips PFH, [1]) is based on fuzzy sets [9]. With every pixel (picture element) a value between 0 and 1 is associated giving the plausibility with which it belongs to a certain image segment. The image segmentation step assigns respective fuzzy membership values to each pixel, such that the resulting segments can be displayed as images with intensity values between 0 and 1, called 'iconic fuzzy sets'. In the approach of P4, the image segmentation is an integral part of an approach to image interpretation and will therefore be described in the next section.

5. Image Interpretation Approaches Followed in COVIRA

In COVIRA, image interpretation was defined as a process in which each picture element is assigned one or more labels according to anatomical terms in the anatomical knowledge base. While the result of the segmentation is a set of regions or contours which have been obtained without the use of the case model, the interpretation approaches make use of this knowledge in order to match the segments to model objects and label them accordingly.

5.1 Image Interpretation Based on Iconic Fuzzy Sets (Partner P4)

For the interpretation approach of P4, each pixel is assigned a list of numbers between 0 and 1, giving the plausibilities with which it receives the label of each of the anatomical terms
for the organs of interest. The image interpretation process consists of three major steps which will be described below:

- A sequence of alternating ‘fuzzy cluster and components analysis’ steps for segmenting the original spin-echo images.
- A ‘fuzzy relational match’ of the resulting segments with the abstract description provided by the case model.
- A display of these interpretation results as coloured overlays of the original spin-echo images.

Fig. COVIRA-9: Result of the P4 interpretation approach for one real clinical case. The various anatomical regions are well segmented and the tumour is clearly outlined in red.

At the top left the original 1st spin-echo image is shown. The top right image displays the final interpretation result with the most plausible membership of pixels being indicated by the brightness of the colour, and the respective degrees of membership by the intensity.

At the bottom left the most plausible memberships are again coded by the brightness of the colour. In this case, however, the respective intensities are given by the intensities of the original 1st spin-echo image. At the bottom right the respective contours of equal memberships in neighbouring anatomical districts are given as colour overlays to the original 1st spin-echo image.
Fuzzified Cluster and Component Analysis

Fuzzy clustering operates in the feature space defined by the two spin-echo images provided, and does not take into account any spatial relationship between organs. The latter are introduced by the recursive procedure by Ohlander [10], which alternates segmentation in feature space and connected component analysis in the spatial domain. The connected component analysis was "fuzzified" by taking the minimal membership along any path joining two pixels as the measure of their fuzzy connectedness [9,11]. The sequence of clustering is aborted as soon as the quotient of fuzzy perimeter and fuzzy area of the resulting components exceeds the value 1.0.

Fuzzy Relational Matching

The segments resulting from the above processing step have to be matched with the symbolic scene description provided by the case model. For that a compatibility graph is generated whose nodes indicate possible matches of data segments with anatomical objects of the case model, and whose edges represent compatible correspondences between them. The final interpretation is then determined as the maximal clique, i.e. the maximal connected sub-graph, in this compatibility graph. To cope with the natural variability of organs and the imperfections of the imaging device (noise, partial volume effects etc.) the matching procedure was fuzzified while avoiding sharp thresholds in order to allow for inexact matching [12,13]. This consistent use of fuzzy sets throughout the image analysis procedure allows uncertainties to be propagated from the classification of individual pixels as belonging to segmented regions up to the labelling of these regions with anatomical terms in the symbolic scene description. Further detail of the approach are given in [14].

Fig COVIRA-9 gives the result of the above approach for one real clinical case.

5.2 Image Interpretation Using a Blackboard Architecture (Partner P2)

Based on the above-mentioned edge/region-based segmentation with region merging after pre-segmentation, Partner P2 (DIBE, Univ. of Genova, [1]) refines the region merging and provides region labelling in a blackboard-based interpretation system. By using some a-priori
knowledge about the anatomical objects expected to be present in the slice, as obtained from the case model knowledge representation, the system is able to reach the final goal as shown in figs. COVIRA-10 and COVIRA-11. The first colour map gives the correspondence between regions and organ labels, and fig. COVIRA-11 displays the contours of the grouped regions overlaid onto one of the original slice images (2nd echo).

The anatomical knowledge used to interpret this image was obtained by analyzing a set of similar slice images, used as a training set, for a refinement of the set of relations between anatomical objects in the case model semantic network representation. Results prove the applicability of this general model to a class of different patients and the effectiveness of the proposed approach.

6. Collection of Medical Data and Manual Segmentation Facility

For the testing of the computer vision prototype demonstrators, clinical data were collected for 20 cases covering:
- statistically significant types of tumors,
- different evolutive forms of the same tumor (from grade I to the aggressive, infiltrating grade IV),
- only hemispheric supratentorial lesions (in view of the restricted anatomical knowledge in the prototypes),
- representative clinical findings and neurological examination data for all patients (for the clinical knowledge input to the case model).

Thus, a preferential selection was made of cases of tumors of neuroglia which are the most common primary brain tumors in human adults, comprising about 40% of all intracranial primary tumors. Furthermore, these tumors are most often in a supratentorial location as required by the prototype demonstrators. Together with the image data, all clinical findings, MR scanner measurement parameters, results of the diagnostic image evaluation and tumor characterizations were documented for each case in a carefully defined protocol.

In order to prepare for the evaluation of the computer vision results by the clinicians, the COVIRA project plan included the building of an interactive computer tool supporting the efficient manual segmentation. The results of the manual segmentation on a number of training cases were presented to the technical partners in order to give a feeling for the relevance of the contours in the image, such that the algorithms could be optimized. This tool was implemented on a standard workstation. It is described in the following.

The purpose of this software tool was to enable the radiologist to perform a manual segmentation of the MR images into relevant anatomical regions. Each of these relevant regions would also be expected to be detected and properly outlined — and properly labelled in case of interpretation — by the computer vision systems. Another goal of this program was to investigate the possibility of user interaction with the automatic segmentation results, using them as support during the manual contour extraction.

The use of this kind of tool during the manual segmentation will provide not only a set of manual contours (to be considered as a 'gold standard' against which the computer vision results could be rated), but also a possibility to evaluate the comparative usefulness of the different computer-determined contours.

The features included in the actual version of the Manual Segmentation Tool (MST) are the following:
- system assisted selection of patient data, images and reference contours,
- basic manipulation of the image appearance such as grey-level windowing and contrast enhancement,
- possibility to calculate derived images by filtering or gradient estimation algorithms,
- point-by-point contour entering, with editing capabilities (insertion and deletion of points) over simultaneous different presentations of the image: simultaneous contour tracking in first and second echo, contrast enhanced or gradient magnitude images etc.,
- zooming of the whole image or cursor-selected areas during the manual editing of the contours,
automatic contour generation, with 'a posteriori' manual edition or validation,
on-line help function, indicating the contours and landmarks previously defined as
standard for the evaluation, and
possibility to incorporate contours or segments extracted from the computer vision results
in order to save time and to allow for an easier
evaluation of their usefulness.

The restricted scope of the COVIRA project did not allow the user interface design to be
fully addressed. As this is a crucial factor in such a very interactive tool, however, the MST
attempts to be user friendly by using a window-based menu and icon-driven scheme.

7. Comparative Evaluation of Segmentation and Interpretation Results
In COVIRA, the above-mentioned different approaches to image segmentation and intepretation have been evaluated in a comparative manner. We summarize: For segmentation, partner P1 has pursued a scheme using a Canny edge detection after taking the average derived from the two MR echo images, followed by a smooth patch fitting for region finding. Partner P2 has pursued a region detection according to Nagao/Matsuyama and used a Marr-Hildreth edge detector based on one of the echoes to guide region merging. Partner P3 has investigated a multiscale approach to edge detection. Partner P4 used a fuzzy clustering approach based on both echoes to provide a fuzzy segmentation of the images.

The image interpretation made use of the case model knowledge. Partner P2 followed a blackboard approach based on the classical low-, middle- and high-level of processing, allowing for a dynamic control with feedback and backtracking mechanisms. Region primitives are recognized and matched to case model objects to check for configuration inconsistencies. Partner P4 performed a fuzzy relational matching based on compatibility between the relations for the regions obtained from fuzzy clustering and those in the semantic net of the model.

For each of these approaches, a prototype demonstrator was implemented. The algorithms were optimized on a number of 'training cases' for which the radiological partner had performed a manual segmentation using an especially developed computer tool. Then a number of test cases were identified on the ground of clinical usefulness and stepwise increased difficulty, and processed by the technical partners. The results were submitted for a comparative evaluation by the physicians based on criteria of usefulness for their clinical tasks.

7.1 Clinical Evaluation of the Computer Vision Results
The final clinical evaluation procedure can be summarized as follows:
1. Four cases were identified by the clinicians in order to test the computer vision results. The selection criteria employed took into consideration different aspects related with neurosciences, neuroradiology, stereotaxy and therapy planning.
2. From the clinical dossiers of the test cases, the information about radiological signs and symptoms was extracted in order for the technical partners to include these data in the generation of the case model.
3. The contours automatically generated by the different computer vision approaches were transferred to the radiological viewing workstation. This allowed to selectively overlay the automatic contours onto the original grey scale MR images.
4. The radiological team then organized an evaluation session in which they performed a manual segmentation of the test case images, making an interactive use of the computer vision results in an attempt to adopt suitable computer-generated contour candidates for the manual segmentation task. During this process, the degrees of usefulness for each of the different computer vision approaches as a support for the manual segmentation task were established.
5. As a result of the evaluation session, each of the manually extracted contours and the automatic contours were carefully compared.
6. A dossier and a comparative table were produced for each technical approach, in which both, the usefulness and the accuracy aspects were documented.
For each anatomical structure which was manually segmented in the image, five main issues (evaluation criteria) were taken into account during the evaluation:

A. **Presence** of the anatomical structure in the computer vision results under consideration,
B. **Quality** of fit of the automatic result with the actual structure as perceived by the radiologists,
C. **Significant local errors** in the automatic segmentation,
D. **False contours** in the automatic segmentation,
E. **Degree of completeness** of the automatic segmentation.

Each of these issues received a semiquantitative score between 1 and 3 according to three different levels of acceptability.

Finally, a **clinical relevance index** was established in order to properly weight the above results from a medical point of view:

Value 0: Results are clinically satisfactory,
Value 1: Irrelevant clinical error,
Value 2: Significant clinical error,
Value 3: Unacceptable clinical error.

An example of the clinical evaluation results is provided in table 1.

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<td>A. Presence</td>
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<td>yes</td>
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<td>B. Quality of fit</td>
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<td>C. Significant local errors</td>
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<td>D. False contours</td>
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<td>E. Degree of completeness</td>
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**Clinical relevance index** 0-1 0 2 2 0 3 3 3 3 0

In fig. COVIRA-12, a selection of automatically and manually determined contours which were generated during the evaluation are displayed.

As the two clinical subcontractors from radiation therapy planning and stereotactic neurosurgery did not have access to suitable workstations, they were asked to provide comments with respect to the usefulness of the computer vision results for their clinical tasks on the basis of paper hardcopies.

The general conclusion from P5 on behalf of the application field of radiology was that some of the results seem to justify further clinical testing already in their current state. For radiation therapy planning as well as stereotaxy, the clinical evaluation showed that in spite of the significant technical advances represented by the computer vision results, their current usefulness is still limited, mainly because, for certain clinical tasks, the accuracy of the organ boundaries is not yet satisfactory. In all cases, the detailed comments were most valuable in providing the technical partners with directions for further improvement efforts.
7.2 Technical Evaluation of the Computer Vision Results

A technical evaluation of the computer vision results was performed on the basis of a blind test of the prototypes in which for an unknown new test case all interaction and parameter tuning activities required were recorded for each of the approaches. The results of this test were discussed along with these records among the technical partners in a workshop which resulted in significant suggestions for improvements of the algorithms and useful combination of the strength of the different building blocks into a unified system approach to be pursued in a forthcoming AIM phase.

8. Recommendations with Respect to Future Activities

The consortium recommends to keep all three application areas in the scope of their future work. In diagnostic radiology, the prototypical interactive segmentation tool should be further evaluated and extended to include quantitative analysis functions. Also for radiation therapy planning RTP and stereotactic neurosurgery SNS, interactive tools shall be realized and tested in a clinical environment, based on state-of-the-art workstation hardware with suitable accelerator boards for fast image processing and 3D display as well as suitable 3D interaction devices. Initial focus will be on interactive approaches using knowledge only for image segmentation purposes. Both RTP and SNS applications require to include CT images, suitable image registration concepts and an extension to 3D. For SNS, the incorporation of DSA and/or MR angiography is required. The results of clinical testing must be subjected to a well designed evaluation procedure.

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