

University of Szeged
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Registration Methods and Their Medical Applications

Summary of the Doctoral Thesis

by

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1 Introduction

There is an increasing number of applications that require accurate aligning of one image with another taken from different viewpoints, by different imaging devices, or at different times. Three consecutive tasks can be defined.

- The process of finding the geometrical transformation that maps a *floating image data set* in precise spatial correspondence with a *reference image data set* is called *image registration*.
- The task of *image matching* is the applying of the found geometrical transformation to the floating image, thus the *aligned image* is produced.
- Using *image fusion*, a brand new image is created from the base and the aligned images, thus their differences or complementary image contents can be visualized and inspected.

Registration can be defined in a more general sense. When the image is taken from an object with exactly known geometry, the mapping between the model and the image can also be established. By summarizing the previous definitions, it can be stated that

- the task of registration is to establish the geometrical correspondence between pictorial and/or geometrical information contents.

Note that the input of registration is sometimes preprocessed, e.g., geometrical or image intensity-based features are extracted from the images.

Registration and image fusion tasks are important in medical image processing. By aligning different images it is possible e.g., to monitor changes in size, shape, or image intensity over time, to combine information from multiple imaging modalities e.g., when relating functional information from nuclear medicine images to anatomy delineated in high-resolution MR or CT images. By relating preoperative images and surgical plans to the physical reality of the patient in the operating room, the surgical intervention can be controlled and monitored, the model of the operating tool can be displayed in the coordinate system of the image. Maintz [16] and Maurer [17] gave extensive survey of this field. Other examples of systems where image registration is a significant component include processing of remote sensed data (e.g., matching a target with a real-time image of a scene for target recognition, monitoring global land usage using satellite images) and computer vision (e.g., matching stereo images to recover shape for autonomous navigation) [5].

Although some of the methods discussed in this thesis could be used to solve problems of other fields, I primarily concentrated on problems arising in the field of medical image processing. The basic definitions, properties and groupings of registration methods are introduced and discussed in Chapter 2.

2 Point-based methods

A general and easily applicable solution for registration problems is selecting points as features. A general point-based method consists of three steps. First, the points are identified, then points in the floating image are corresponded with points in the reference image, finally a spatial mapping is determined. The transformation that aligns the point sets best is then used

to align the images. In Chapter 3, the properties and search steps of rigid-body, affine, perspective, polynomial, and thin-plate spline (TPS) transformations are introduced. The affine transformation is discussed in more detail.

2.1 Search for affine transformation

An affine transformation maps straight lines to straight lines preserving parallelism, but angles can be altered. This can be achieved by applying translations, rotations, non-uniform scalings and shearing transformations. Each $\mathcal{T} : \mathbb{R}^k \rightarrow \mathbb{R}^k$ k -dimensional ($k = 2, 3, \dots$) affine transformation can be described by a matrix of size $(k + 1) \times (k + 1)$,

$$T = \begin{pmatrix} t_{11} & t_{12} & \cdots & t_{1k} & t_{1,k+1} \\ t_{21} & t_{22} & \cdots & t_{2k} & t_{2,k+1} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ t_{k1} & t_{k2} & \cdots & t_{kk} & t_{k,k+1} \\ 0 & 0 & \cdots & 0 & 1 \end{pmatrix}.$$

For $x = (x_1, \dots, x_k)$ and $y = (y_1, \dots, y_k) \in \mathbb{R}^k$ we have $y = \mathcal{T}(x)$ if and only if $y_H^T = T \cdot x_H^T$, where x_H and y_H denote the homogeneous coordinate representation of the points. This kind of transformation has $k \cdot (k + 1)$ degrees of freedom according to the matrix elements to be determined.

Let $\{p_i\}$ and $\{q_i\}$ denote the two corresponding point sets in \mathbb{R}^k where $p_i = (p_{i1}, \dots, p_{ik})$ and $q_i = (q_{i1}, \dots, q_{ik})$, and let $p'_i = T(q_i)$ ($i = 1, 2, \dots, n$). We need a transformation \mathcal{T} which takes points $\{q_i\}$ exactly to $\{p_i\}$, i.e., $p'_i = p_i = T(q_i)$ ($i = 1, 2, \dots, n$). Thus we get a system of $n \cdot k$ equations in the form of

$$A \cdot \mathbf{t} = \mathbf{b} \quad (1)$$

where the number of unknown elements is $k \cdot (k + 1)$. It can be seen that the necessary (but not sufficient) condition of the unique solution is that we have at least $k + 1$ point pairs. Having more point pairs than that, the system will be overdetermined — such a system often doesn't have any solutions. If this happens, we can determine the result in the least squares sense. This solution minimizes the Euclidean norm of the vector $(\mathbf{b} - A \cdot \mathbf{t})$:

$$\psi(t_{11}, \dots, t_{k,k+1}) = \sum_{i=1}^n \|p'_i - p_i\|^2 = \sum_{i=1}^n \sum_{j=1}^k (t_{j1} \cdot q_{i1} + \dots + t_{jk} \cdot q_{ik} + t_{j,k+1} - p_{ij})^2. \quad (2)$$

Function ψ may be minimal if all of the partial derivatives $\frac{\partial \psi}{\partial t_{11}}, \dots, \frac{\partial \psi}{\partial t_{k,k+1}}$ equal to zero [23]. It was shown that if q_1, \dots, q_n spans \mathbb{R}^k , the solution of (2) is unique. In practical applications it means that in 2D we need at least three non-collinear, in 3D four non-coplanar point pairs. Furthermore, we gave a 3D example illustrating the existence of a degenerated solution.

2.2 Error analysis of point-based methods

Since the alignment of the images is indirect when point-based methods are considered, it is important to determine how the identification of point pairs influences the actual registration error. What happens if more and more point pairs are selected? What is the effect of the

localization error of the points? What role the orientation and position of the points play? If there are many solutions for a given problem, which should we choose? Which is the faster or more stable in numerical sense? This topic is discussed in detail in Chapter 4.

When examining the error of point-based registration in medical image registration problems, the fiducial (point) localization error (FLE), the fiducial registration error (FRE), and target registration error (TRE) are considered (Fig. 1) [18].

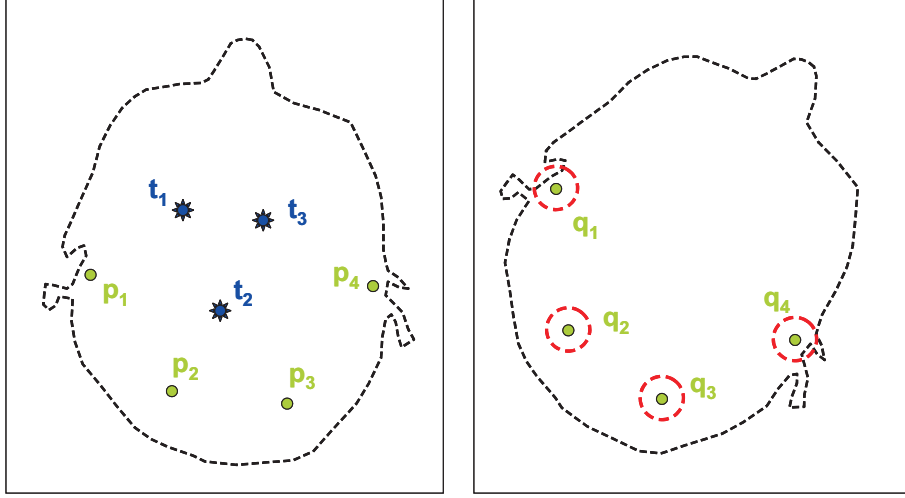


Figure 1: The localization of q_i points corresponding to p_i is prone to smaller or bigger errors (FLE). A point-based registration method optimizes the alignment of these erroneously selected point pairs (FRE). We are interested in the registration error of the points t_i in the target region (TRE).

In practical applications only FRE is available for use. FLE and TRE play an important role in the theoretical examination of transform type and search method properties. When an approximation is given to the localization error, it is possible to examine the effect of different parameters using numerical simulations. Many papers from several research groups investigate rigid-body transformations, which is undoubtedly the most popular transformation type. The following important statements were deduced.

- For a given number of point pairs, TRE is proportional to FLE [7, 19].
- TRE is approximately inversely proportional to the square root of the number of point pairs [15, 19].
- TRE models the actual registration error more reliably than FRE which can be misleading [14].

Besides rigid-body, we focused on affine transformations also [24, 25]. We investigated the following four methods: The rigid-body method proposed by Arun et al. (RB1) [1], our implementation of an iterative rigid-body method utilizing the Levenberg-Marquardt nonlinear minimization method (RB2) [27], our affine search method (LIN) [23], and the thin-plate spline (TPS) non-linear method proposed by Bookstein [4].

The effect of point localization error

The first investigation was related to point localization. The iteration was executed 100,000 times by selecting the standard deviation of the noise parameter from the [0.0,5.0] interval

assuming normal distribution of it. The simulation was executed for fixed rigid-body and affine transformations, and also for randomly generated transformations at each iteration steps. The same results were obtained for both cases. It was concluded that TRE is proportional to FLE when the number of point pairs is fixed, for both rigid-body and affine transformations and for all the four search methods. It was confirmed that when there is a rigid-body motion, it is not worth searching for a more general transformation type since the localization error can introduce false deformations which degrades the alignment. When comparing FRE and TRE , it is prominent that TRE models the actual registration error more reliably than FRE .

The effect of the number of point pairs used

The topic of the second experiment was the inspection of the number of point pairs used. The simulation was similar to the previous one. Here, the number of point pairs were selected from the 5–200 interval. It was concluded that for methods RB1, RB2 and LIN TRE is inversely proportional to the square root of the number of points used above a given number of points. It holds for rigid-body methods roughly when $N > 6$, for affine methods when $N > 10$. If less point pairs are used, the error decreases faster. An interesting effect is visible in case of the TPS transformation. For a given number of points the inversely proportional property is fulfilled, above that the error increases dramatically.

The effect of the positions of the points

This effect was first studied by Maurer et al. [19]. We made a new type of experiment, investigating the effect of the volume spanned by the point to the registration error. It was concluded that TRE is inversely proportional to the volume measure in case of both rigid-body and affine transformations. Note that for affine transformations with scaling parameters that cause a significant change in the volume, the model of FLE may not remain realistic.

Spatial distribution of TRE

Naturally, TRE is not constant in every position — it strongly depends on its relative position to the selected points. Maurer observed that for rigid-body transformations, the expected error is minimal at the centroid of the selected points [19]. The bigger the distance from this centroid the bigger the error. The same error values can be found at same distances from the centroid. We made investigations related to the 2D affine case, which confirms the previous statement also in this case.

Examination of fixed point configurations

In medical applications where point-based registration is used routinely, it is worth determining those set of points that are well visible and can be selected unambiguously in the given image modalities. Thus, the user can follow a fixed protocol which can speed up the process of point selection. We investigated the alignment of MR images. A clinical expert named 13 suitable anatomical points. By applying numerical simulations, the relevance of the points was investigated. We tried to answer the question whether it was possible to achieve acceptable results by selecting less points. Based on these investigations an easily applicable and under-stable strategy was proposed for the number of points to be used and their selecting order.

It was observed that the positions of the points relative to each other and to the region of interest play a very important role. As a natural rule, it is worth selecting more and more point pairs, but it is also well visible that “good” point configurations of 4–5 points can produce similar errors to that of even 9–10 points. By selecting the most relevant 8–10 points the

alignment is almost as good as using all of them. By selecting 7 or less points randomly, the error can be unacceptably big even if the volume spanned by the points seems to be large enough.

Our first approach to determine the relevance of points takes into account those points that can be found in the best configurations, the second investigates the goodness of configurations the points take part in on the average. Our proposal for the order of selection of points is the following: At first, start selecting points in the order determined by the best configurations. If it is not possible to identify a point, let's select the most reliable points from the average relevance list.

3 Automatic registration

Automatic registration methods are the easiest to use. However, visual inspection of the result is always necessary since these methods often cannot judge whether it is acceptable. We can distinguish between two approaches. In the first case geometrical information contents (e.g., corner points, contours, surfaces) are extracted from the images and these are used for registration. In the second case the image intensity values are used directly utilizing *voxel similarity measures*. In the thesis, the latter case is investigated.

3.1 Registration method

We proposed a fast, fully automatic registration algorithm that is capable of solving unimodality or multimodality registration problems in 2D or 3D. Many similarity measures were proposed in the past decade. We chose the measures based on the mutual information of the images proposed by Collignon et al. [6] and Viola and Wells [34], and on the normalized mutual information of the images proposed by Studholme et al. [20].

To speed up the registration process and to avoid falling in local minima during search, we used the Gauss pyramid representation of the images. The search starts at the coarsest level. When an optimal result is reached, this is used to initialize the next, finest level. We use Powell's direction set, iterative, nonlinear optimization algorithm to find the optimum of the similarity measure. This method requires evaluating the similarity measure value for given transformation parameters only, no gradient or other information is necessary. The most time consuming part of the process is the execution of the transformation. We utilized many optimizations, e.g., multiplications were superseded by summations, mutual information was reformulated for less computations and a look-up table was used to get logarithmic values. The detailed descriptions of these optimizations can be found in Chapter 5.

3.2 Evaluation of MR-CT and MR-PET registration

To evaluate our registration method, we joined the Retrospective Registration Evaluation Project of Vanderbilt University, USA in 1999 [36]. The objective of that project was to perform blinded evaluation of retrospective image registration techniques using a prospective, marker-based registration method as a gold standard.

The steps of evaluation were the following. Image volumes of three modalities: X-ray computed tomography (CT), magnetic resonance (MR), and positron emission tomography (PET) were obtained from patients undergoing neurosurgery at Vanderbilt University Medical Center, on whom bone-implanted markers were mounted. These volumes had all traces of the

markers removed and were provided to project collaborators outside Vanderbilt, who then performed registration on the volumes. The investigators communicated their results to Vanderbilt, where the accuracy of each registration was evaluated.

Two registration tasks were evaluated: CT to MR and PET to MR, and these tasks were broken into subtasks according to the type of MR and to whether or not the MR image was corrected (rectified) for geometrical distortion. The image data set of nine patients were used, seven of which contained both CT and MR, and seven with both PET and MR.

The results of the project were published in [36] and [35]. Since we joined the project later, our results were not included in those papers. That's why we compared our results against those evaluated earlier [28]. Ten groups of investigators applied 14 techniques to solve the registration tasks. The techniques were divided into two groups. Six of the 14 techniques were volume based and eight were surface based. Our methods can be classified as volume based ones.

Before the evaluation of our results, we visually inspected the quality of registration. When the normalized version of the mutual information (NMI) was used, all registration results were visually acceptable. In case of mutual information (MI), the results were visibly misregistered for four image pairs of PET-MR problems. In spite of these clear misregistrations, all results were submitted for evaluation to Vanderbilt University. Table 1 shows the statistics of registration errors for the groups of algorithms, and the rankings of our methods out of the 16 competing methods.

Modality	Surface based mean error (std.dev.)	Volume based mean error (std.dev.)	Our MI mean error (ranking)	Our NMI mean error (ranking)
CT-T1	5.7 (7.8)	2.9 (2.4)	1.6 (#2)	2.3 (#7)
CT-PD	5.8 (8.0)	2.9 (2.5)	2.2 (#2)	1.8 (#1)
CT-T2	6.3 (7.9)	2.4 (1.4)	2.0 (#5)	2.0 (#3)
CT-T1 rect.	6.1 (8.3)	2.0 (2.5)	1.7 (#5)	2.2 (#7)
CT-T2 rect.	5.7 (7.8)	1.8 (2.0)	1.4 (#3)	2.3 (#7)
CT-PD rect.	6.1 (7.6)	2.1 (1.6)	1.7 (#4)	2.4 (#7)
PET-T1	3.9 (2.0)	3.5 (2.1)	5.3 (#9)	3.0 (#2)
PET-T2	4.4 (2.1)	3.6 (1.9)	3.8 (#7)	3.5 (#4)
PET-PD	4.3 (2.6)	4.0 (2.7)	4.4 (#7)	4.2 (#10)
PET-T1 rect.	3.9 (2.3)	2.7 (1.4)	3.8 (#12)	2.7 (#3)
PET-T2 rect.	3.9 (2.0)	3.5 (1.7)	3.9 (#10)	3.3 (#5)
PET-PD rect.	3.9 (2.3)	3.5 (2.4)	4.8 (#10)	3.0 (#2)

Table 1: Mean and standard deviation of registration errors. Note that the rankings of our methods are based on the median errors of the registration methods, as it was published in [36].

The results show that in case of CT to MR registration task, both of our methods produce acceptable results. Our MI method produces good, our NMI method average results. For PET-MR problems, the MI method tends to fail (four failures out of 35 cases), and that's why it produces average results. The NMI method gives stable results and ranks high among the competing algorithms. The running time was about 30–120 seconds on a 800 MHz Pentium-III

PC. More detailed results of the evaluation of our methods can be found at <http://www.vuse.vanderbilt.edu/~images/registration>.

3.3 Registration in a segmentation framework of pelvic CT images

The method was tailored to the needs of a model-based segmentation framework of the pelvic area in CT studies in collaboration with GE Medical Systems. Registration was used as a pre-processing task. The goal of it was the acceptable alignment of the pubic bone area (where the two organs of interest, the prostate and bladder are located) of studies from different patients [30–32].

The method was used in the following two tasks. The collected CT studies were transformed to a common reference frame by selecting a suitable study and using it as a reference. Then a statistical atlas was computed which shows how probable it is that the given voxel belongs to a specific organ for each voxel of the reference frame. Manual segmentation was necessary to build the atlas, which was carried out by three experts. The second task occurs in the clinical software, where the statistical atlas information is transformed to the coordinate system of the image to be segmented for initialization of the segmentation method. A deformable organ model could also be used instead of the statistical atlas. The scope of our discussion was the role of registration as a preprocessing step, we did not deal with deformable organ models at this point.

The applied algorithm consists of two steps (Fig. 2). The idea is that after a transformation having translational, rotational and non-uniform scaling parameters which gives global optimal alignment, a refinement step is performed. Global registration prefers alignment of body parts of big volume, like spine or pelvis, causing slight or big differences in the pubic bone area. It is assumed that scale parameters are satisfactorily determined by this global part. During refinement, scale parameters are kept from the global part, then an optimal rigid-body transformation is searched in the pubic bone region only. The refinement requires the manual selection of the local neighborhood of the pubic bone in the reference study.

It was shown that our proposed two-step method (local refinement in the pubic bone area after a global registration) takes prostate regions significantly closer to each other when transforming to the common reference frame. GE Medical Systems provided us with an image database of 26 CT studies and their expert segmented prostate and bladder regions. In our database the failure rate of registrations was low (three out of 26) even though the studies were “real-life”, many of them distorted by metallic objects, or not satisfying the assumed protocol (e.g., wrong patient position, contrast agent is visible in the images). Utilizing several optimizations (e.g., by using only the coarser levels of a hierarchical representation), the running time is currently between 20–40 seconds on a 3 GHz Pentium IV desktop PC. It can be further reduced to nearly its half by reducing the number of voxels in the reference volume removing the unnecessary parts (e.g., using the bounding box of the patient data).

3.4 Application in neutron tomography

The registration method was used in an interesting, non-medical problem [2]. Neutron radiography provides more contrasted images than conventional X-ray based techniques when examining the inner parts of objects made from iron, copper or aluminium. As it passes through the objects, the neutron ray is absorbed to some extent. The remaining intensity of the ray is measured by an imaging plate, thus we can get the projected image of the object. By rotating

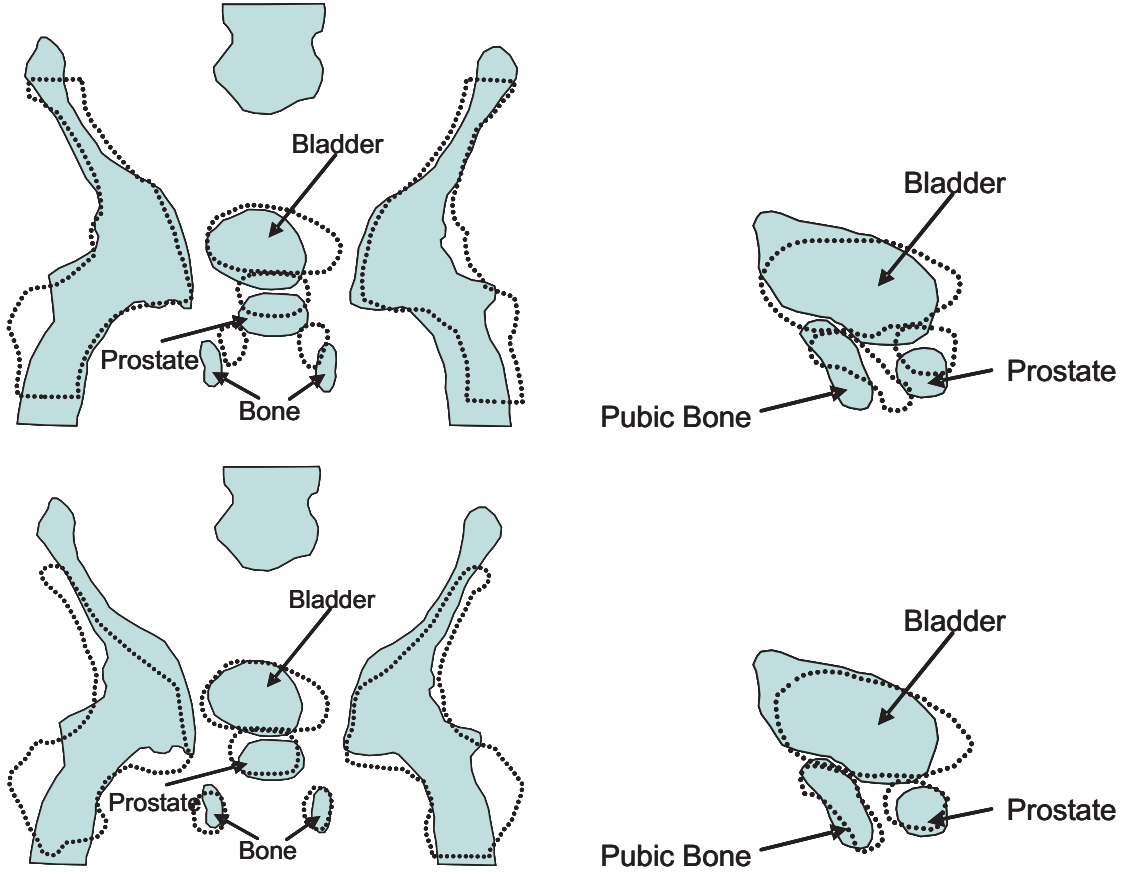


Figure 2: Top row: The optimal global registration of a study (*dotted outline*) against the reference volume (*filled shape*) — a coronal (*left*) and a sagittal cross section (*right*). It is well visible that the organs of the two studies are close to each other, but the overlapping region e.g., of the prostate, is small. Bottom row: The optimal local rigid-body refinement following the global registration of a study against the reference volume — a coronal (*left*) and a sagittal cross section (*right*). The result of the registration provides a good starting point for a segmentation algorithm. The figures are derived from real data.

the object, a series of 2D projections is produced from which the 3D model of the object can be calculated using tomographic methods.

The way the images are taken introduces geometric differences between the consecutive projections. It means that the same projection directions from the source might pass the imaging plate at different pixel locations. Such geometric differences can degrade the result of the reconstruction. Image registration is applied to recover these geometric differences.

The main reason of error is the fact that the removing and reinserting the imaging plate can cause translational and rotational differences. To eliminate the rotational invariance, artificial markers are affixed in front of the imaging plate, the projections of which are visible in the top, bottom, left and right hand side of the images.

We used the 2D version of our method based on normalized mutual information. It is assumed that a rigid-body transformation (translation along the axes and rotation about the center of the image) can align the images. Although the algorithm is fully automatic, a pre-processing step is necessary. The center region of the images, where the projection of the object is visible, must be masked out and the similarity measure is evaluated only outside of

it. One of the projection images is selected as the reference image and the others, including the open beam projection image, are registered against it one by one.

Visual inspection confirmed that the markers aligned well after registration and that the reconstruction using the registered images produced 3D images of better quality.

4 Image-guided planning and execution of percutaneous therapies

The images taken from the patient can be of great use to therapy planning and execution also. Registration plays an important role here also: The geometrical relationship between the physical space and the image coordinate systems must be determined, thus it is possible to track the movement of the device with respect to the image of the patient and it is even possible to control it to hit target points.

In case of percutaneous therapies — such as biopsy, brachytherapy, nerve blocking, radio frequency ablating — there is an increasing demand for minimal invasiveness [8, 9]. Their advantages include less trauma for the patient, faster recovery from illness, fewer complications and lower cost. However, the reduced visibility of the target area and the lack of room to maneuver are disadvantages for the surgeon. Image guidance help to overcome these problems.

A possible approach is that 3D images are taken from the patient preoperatively and/or during the operation. The images are transferred to a computer where the surgeon makes the plan of the operation: What the entry points are, in which direction and to what depth the needle should move. By displaying the planned needle trajectories together with the images, it can be decided whether they are viable: Whether any of them hit any critical anatomical areas, such as arteries or bones. The accepted plan can be executed and — if it is necessary — postponed or stopped from the planning computer. After the intervention another image can be taken for verification. If it is necessary, a new intervention can be planned and executed the same way. This is the so called “Point and Click” paradigm that is used generally for percutaneous therapies at the Johns Hopkins University (MD, USA).

4.1 Percutaneous therapies using localization frames

The planning and execution of percutaneous therapies are very diverse. First those are investigated that make use of a *localization frame*. When using a so called *stereotactic frame*, a base is rigidly attached to the patient that provides the coordinate system. Execution can be done using robots when the localization frame is attached rigidly to the robot itself. The assumption is that the given device is able to rotate the needle around a fixed point (often it is the tip of the needle), insert it to a given depth and retract it. The spatial movement of the needle is not necessary but might be useful.

The localization frames contain rods which are well visible in the image together with the patient and their geometry provides that the solution is unique even if only one image slice is available. Although the build-up of the devices can be very diverse, their operational principle is very similar. Three objects can be distinguished which are defined in their own coordinate systems. The first is the patient represented by the images taken of him/her, the second is the needle or tubular device that is to be inserted, and the third is the localization frame. The task of registration is to establish the geometrical correspondence between these coordinate systems (Fig. 3).

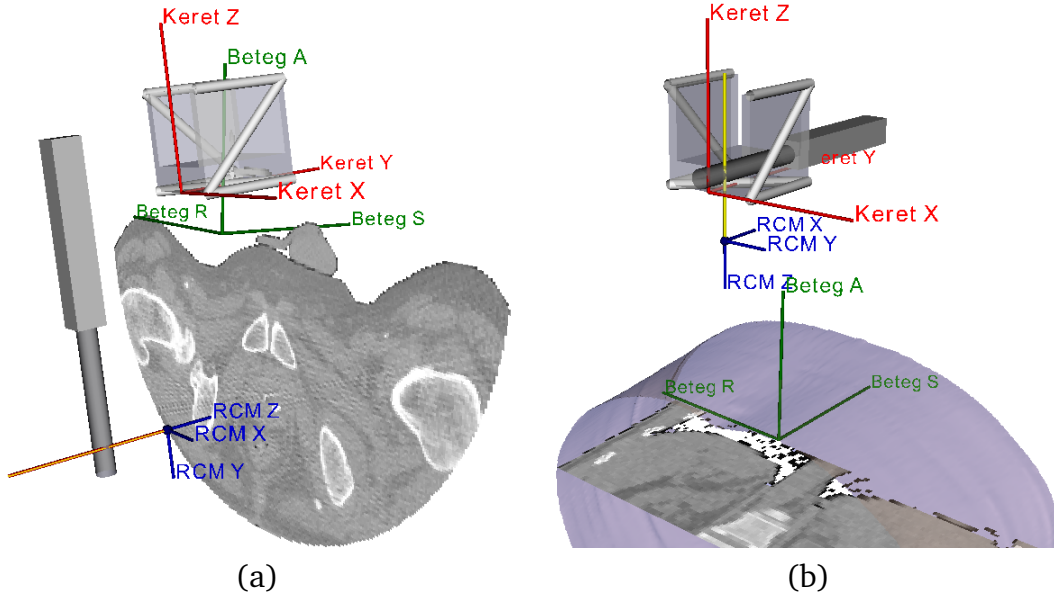


Figure 3: Correspondence between the coordinate systems of the patient, the frame and the operating device for different robot configurations after registration. The coordinate systems are labeled as “Beteg”, “Keret” and “RCM”, respectively in the images (a) and (b).

We developed an iterative registration algorithm where the rods are modelled with line segments, the centroids of the rod intersections in the images are identified manually or semi-automatically and registered to the line segment models in the least-squares sense [29]. Even a single image slice containing some intersections of the rods can be sufficient for the unique solution. More rod intersections and more image slices available make the precision of registration much better. The algorithm requires the specification of which set of points represents which rod.

The effect of point localization error to the registration error was investigated using numerical simulations. We compared our method with the one proposed by Susil. That algorithm requires only one image slice [21]. Based on the results, the error of the iterative method is smaller than that of Susil’s direct method even when only one slice is used. Significant improvement can be detected even when two slices are used. The only deciding factor according to which the direct method is undoubtedly better than the iterative one is the running time. However, because of the nature of the practical problem (the selection of the rod intersection points is far more time consuming than the registration method itself which is less than one second) the application of the iterative method can also be a viable solution.

When the geometrical relationship between the three coordinate systems is established, the planning and execution steps of the therapy can be given in a unified framework. It is referred to as *abstract control level*, since it is not necessary to know what the actual physical device is and how it works. The abstract movement parameters are computed at this level. The task at the *physical control level* is the actual execution of the operation. This can be done when the inverse kinematics of the device is known.

I developed a therapy planning and controlling application based on this framework. CT scans are taken from the patient, the RCM robot family is controlling the needle to which the Susil-frame is rigidly attached. Pre-clinical phantom experiments were designed to prove the basic feasibility of this system [9]. The results showed that the primary source of error is attributed to the interaction between the patient and the needle. In real situations the move-

ment of the prostate during needle insertion and the movement of the patient after the CT image is taken can cause problems. Although these problems might be handled, we assumed they are negligible. Results of preliminary experiments indicate that the robotic system may be suitable for transperineal needle placement into the prostate and shows potential in a variety of other percutaneous clinical applications.

4.2 Other percutaneous therapies

During my study trip to the Johns Hopkins University (MD, USA) I took part in two other projects in which registration plays an interesting and important role.

In the first one we unified the advantages of three systems: ultrasound-based systems that are generally used in clinical settings, computer-assisted 3D therapy planning systems using robots and MR imaging, for percutaneous therapies of the prostate. The target area is well visible in the MR images upon which the therapy is planned and the robot is controlled. The robot approaches the prostate via the rectum. During the therapy, 2D MRI images are taken and displayed in real-time. The work was divided into several parts [3, 10, 11, 13, 22]. My task was the displaying of the 2D real-time images and I took part in the planning of the communication layer between the scanner and the planning computer.

In the second project my task was to develop the communication layer between a commercially available ultrasound-based brachytherapy system and a robot capable of executing percutaneous therapies, and I took part in the planning of calibration between the two systems [12].

5 Contributions of the thesis

Contributions in the first group are related to the examinations of point-based methods. Their detailed discussion can be found in Chapter 3 and Chapter 4. The results were published in journal articles [23, 26, 27] and conference proceedings papers [24, 25].

- I/1. I reviewed the search steps of rigid-body, affine, perspective, polynomial, and TPS transformations in a unified framework and summarized their properties [27]. We proposed a new affine search method based on the examination of the partial derivatives of the cost function [23], and gave and proved a sufficient existence condition for the unique solution. We also gave a 3-dimensional example for the existence of the degenerated case.
- I/2. I performed the error analysis of the point-based methods using numerical simulations. I determined that the expected target registration error is
 - (a) proportional to the fiducial localization error assuming affine motion,
 - (b) approximately inversely proportional to the square root of the number of point pairs assuming affine motion,
 - (c) inversely proportional to the volume spanned by the points assuming rigid-body and affine motions,
 - (d) constant in iso-ellipses around the centroid of the point sets in 2D assuming affine motion,

and I gave a strategy for determining the number of point pairs to be used and their selecting order.

Contributions in the second group are related to automatic registration and its applications. Their detailed discussion can be found in Chapter 5. The results were published in a journal article [28] and conference proceedings papers [2, 30, 31, 33]. There is also a related patent application [32].

- II/1. I proposed an automatic, voxel similarity-based multiresolution registration algorithm. With methods based on mutual information and normalized mutual information, we took part in the retrospective image registration evaluation project conducted by Vanderbilt University and achieved good results [28].
- II/2. The method was tailored to the needs of two preprocessing steps of a segmentation algorithm of the pelvic area: in determination of statistical organ models and their initial placement in the clinical software. It was shown that the local refinement of the global registration result in the neighbourhood of the pubic bone takes the prostate regions significantly closer to each other [30–32].
- II/3. We used the 2D version of the algorithm to reduce the geometrical differences of neutron radiographic projection images, which is a necessary preprocessing step of the tomographic reconstruction [2, 33].

Contributions in the third group are related to a computer assisted surgery planning and controlling task. During my study trip to Johns Hopkins University I worked on minimal invasive percutaneous therapies.

- III/1. In case of therapies utilizing localization frames
 - (a) I proposed a unified framework based on the point-and-click paradigm,
 - (b) I proposed a registration method for registering rod intersections identified in the image and their models,
 - (c) I performed the examination of the effect of the localization error in case of the Susil-frame using numerical simulations,
 - (d) I prepared a treatment planning and execution application that utilizes CT imaging and a robot with the Susil-frame rigidly attached for percutaneous procedures of the prostate and abdominal organs.
- III/2. I contributed to the initial work of the following projects.
 - (a) In a transrectal percutaneous system utilizing MRI imaging I elaborated the visualization of the real-time 2D images and we planned the communication between the scanner and the planning computer.
 - (b) I elaborated the communication between an ultrasound-based brachytherapy system and a percutaneous robot and participated in the planning of the calibration of their coordinate systems.

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