

*registration, optimization methods, visualization,  
virtual patient-specific anatomical models,  
Visible Human Project dataset*

Michał CHLEBIEJ<sup>\*</sup>, Zdzisław KRÓL<sup>\*\*</sup>, Paweł MIKOŁAJCZAK<sup>\*</sup>

## **NUMERICAL TREATMENT OF REGISTRATION PROBLEM IN GENERATION OF PATIENT-SPECIFIC ANATOMICAL MODELS**

Registration is an important component of many medical data processing applications. Particularly significant is its role in the correlation of volumetric medical data aiming at generation of virtual patient-specific anatomical models. Such models enable optimization of various diagnostic and therapeutical procedures. The importance of the virtual patient models is becoming increasingly recognized in modern medicine. The advantages of using such biomedical virtual models are analogous to the advantages of real system behavior simulation in the engineering or material sciences. In this work some numerical issues associated with the registration problem and the visualization challenges arising in the context of virtual anatomical models have been presented and discussed.

### 1. INTRODUCTION

Sophisticated image processing methods for 3D medical images are of considerable importance to the effective use and understanding of medical imagery in many applications, particularly in those requiring accurate representation of anatomical structures like diagnosis, therapy planning and simulation. A large number of algorithmic techniques for reconstruction, segmentation, registration, visualization and other image processing methods have been reported in the literature [1]. One of the most exciting challenges in this area of research is how to integrate diverse forms of raw and processed information towards a common information framework. Tomographic images of different modalities, and outcomes of the above mentioned image processing methods provide structural input to such framework called in the literature as the virtual patient-specific anatomical model. Such models provide many advantages for diagnostics and treatment planning, particularly in the radiation therapy or for complex surgical procedures. The virtual patient-specific anatomical models enable enhanced perception of the region of interest as well as simulation of the surgical or radiation treatment and the evaluation of potential scenarios. The registration approach plays an important role in the generation of the virtual anatomical model for the patients undergoing two or more imaging studies. Because the acquisition of the data is procedurally and technologically independent, the complementary information provided by

---

<sup>\*</sup> Pracownia Technologii Informatycznych, Maria Curie-Skłodowska University, Faculty of Mathematics, Physics and Informatics, pl. Marii-Curie Skłodowskiej 1, 20-030 Lublin, Poland. E-mail: meow@goblin.umcs.lublin.pl

<sup>\*\*</sup> Surgical Simulation and Navigation Group, caesar - center of advanced european studies and research, Friedensplatz 16, 53111 Bonn, Germany. E-mail: krol@caesar.de

different imaging modalities has to be correlated by means of numerical methods. The usability of the complex virtual patient models depends strongly on efficient visualization methods that enable exploration of such huge amount of data. This paper is organized into two main sections: numerical issues associated with the registration method, and generation and visualization of the virtual anatomical model. The related results and problems will be discussed at the end of the work.

## 2. REGISTRATION FOR VIRTUAL ANATOMICAL MODELS

The registration along with the segmentation task belong to the major efforts in the process of generation the patient-specific virtual anatomical model. The registration problem induced by the fact that two datasets of the same patient taken in one modality at different times or in more than one modality differ with respect to resolution, acquisition plane, or parameter measured. Before they can be used in conjunction with each other, it is first necessary to register or correlate geometrically these two or more sets of data (see Figure 1). Because of the above differences the process of spatial alignment is not trivial. To solve this problem using numerical methods we have to define a geometrical transformation relating the two data sets as well as a criterion for the goodness of a given transformation. We treat the registration problem as a non-linear optimization task aimed at the minimization of the dissimilarity measure.

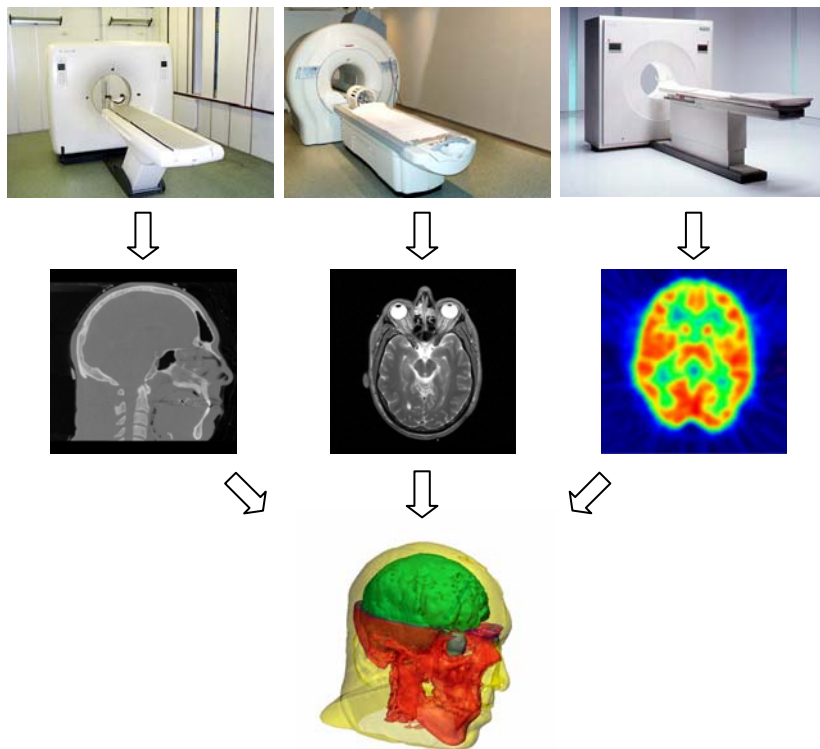


Fig.1. Generation of the virtual patient-specific anatomical model. Top line (left to right): CT, MR and PET scanning devices delivering complementary diagnostic information. Middle line: individual slices from the volumetric datasets acquired from the above presented devices. Bottom: virtual patient-specific anatomical model generated from the multimodal datasets (brain is yielded from the MR dataset, and bones and skin from the CT dataset).

2.1. FORMAL STATEMENT OF THE REGISTRATION PROBLEM

To provide the basis for more technical description of the registration problem and the associated concepts we define the similarity measure  $C$  as the objective function, which has to quantify how well the two datasets (let us call them model and object) match with each other. The matching transformation  $\mathbf{T}$  is defined as a geometric transformation that takes a point  $p_o$  of the object volume and gives its anatomically equivalent and unique model point  $p_M$ . The majority of registration methods share a common optimization framework, where the goal is to estimate numerically the optimal transformation  $\mathbf{T}_v$ , which establishes the anatomically optimal spatial correspondence between the model and the object. In case of rigid body transformation (six degrees of freedom)  $v=[r_x r_y r_z t_x t_y t_z]$  is a six-component vector, which has to be estimated. Many different registration methods have been proposed in the literature [2]. In this work, from the most representative similarity measure classes two similarity functions have been chosen. The first one is the surface similarity measure:

$$C(v) = \sum_{i=1}^N d^2(\mathbf{T}_v(p_i)) \quad (1)$$

where  $d(p)$  is the Euclidean distance in  $\mathfrak{R}^3$  between any transformed object point  $p = \mathbf{T}_v(p_o)$  and some closest to  $p$  model data point  $p_m$  and it denotes the length of the vector that is defined by this pair of points:  $d(p) = \|p - p_m\|$ .  $N$  is the number of the segmented object points. The second similarity function is the mutual information measure:

$$C(v) = - \sum_{g_i \in G_o} \sum_{g_j \in G_M} P(g_i, g_j) \log \frac{P(g_i, g_j)}{P(g_i)P(g_j)} \quad (2)$$

where  $P(g_i, g_j)$  is a probability distribution of the scatter-plot histogram [2], and the  $P(g_i)$ ,  $P(g_j)$  are the probabilities for each object and model gray-value in the intersection volume.  $G_M$  and  $G_o$  are the gray-value sets of the model and object volumes. Both similarity measures represent different approaches to quantify the similarity between two datasets. The first one is taking into account features identified in a non-automatic segmentation step (at the preprocessing stage). The second one uses the whole gray-value information from both datasets and works without any preprocessing stage. Unlike the surface similarity approach, where the similarity assessment takes place in Euclidean space, the mutual information measure works in a different mathematical space and estimates the distance between the probability distribution of the scatter-plot histogram  $P(g_i, g_j)$  and distribution  $P(g_i)P(g_j)$  of two independent signals.

In this work our main interest is focused on the optimization task related to the registration problem. There is a plenty of different numerical optimization methods [3]. To choose the most adequate one for a specific class of registration problems, one has to consider a few important factors. Assessing the match quality in the continuous Euclidean or probabilistic spaces determines the continuous nature of the registration problem for the volumetric medical data. The nonlinear nature of

the matching functions and the existence of local minima has been described in the literature [2]. Because of the huge size of the datasets, computation of the objective function value or its derivatives is a very time consuming part of the whole optimization process. The existence of local minima requires applying global non-deterministic optimization methods [2]. But in this class of methods a high number of objective function calculations are often necessary to satisfy convergence criteria, what is impractical in the case of medical data registration. In opposite, there exists a wide group of much less time consuming, deterministic algorithms. Depending on the kind of objective function we may use different deterministic optimization techniques. If we are only able to compute the value of the function for a given set of variable parameters and we cannot even estimate its gradient we may use Powell's method [3]. In cases when we are able to compute something more than just a function's value we can choose a few numerical techniques that follow the simple nonlinear optimization solution. The simplest method, gradient descent (or ascent) just follows the gradient of the objective function until it hits a local minimum and then stops [3]. Some more recent methods for solving optimization problems methods like Davidon-Fletcher-Powell [3] or Levenberg-Marquardt [4] try to estimate or compute second derivatives of the objective functions. With this information, local areas of the objective function can be approximated quadratically for the better convergence properties. With deterministic methods for highly nonlinear optimization problems, the absolute best solution is not always guaranteed unless we start close to it. In this work two deterministic methods have been chosen: the Levenberg-Marquardt optimization scheme for the surface similarity measure and the Powell's method for the optimization of the mutual information based objective function. The next sections contain a short description of these nonlinear minimization techniques.

## 2.2. LEVENBERG-MARQUARDT OPTIMIZATION METHOD

The Levenberg-Marquardt optimization scheme is a standard nonlinear least-square technique that works very well in a wide range of situations. It provides a way to vary smoothly between the Gauss-Newton method and the steepest descent method. The Gauss-Newton optimization method is specifically designed for minimizing the objective function, which has the form of sum of square functions, such as the surface similarity function. One of the most important features of Gauss-Newton optimization method is the very fast convergence, but the method converges only close to the optimum. The method of steepest descent is the simplest of the gradient methods. The choice of direction is where  $C(v)$  decreases most quickly, which is in the direction opposite to  $\nabla C$  (gradient of  $C(v)$ ). The search starts at an arbitrary point  $v_0$  and then slides down the gradient, until we are close enough to the solution. The method of steepest descent is simple, easy to apply, and each iteration is fast. If the minimum points exist, the method is guaranteed to locate them after at least a finite number of iterations. But, even with all these positive characteristics, the method has one very important drawback - it generally has slow convergence.

## 2.3. POWELL'S OPTIMIZATION METHOD

The Powell's method is a single-shot method, which attempts to find the local fit statistics minimum nearest to the starting point. The main advantage of this numerical technique is that it is a robust direction-set method. Algorithm minimizes the function in one coordinate direction, and then from there it moves along the next direction until a minimum is reached. The method is cycling

through the whole set of directions until the fit statistics is minimized for a particular iteration. After that process the set of directions is updated and the next iteration proceeds. The procedure continues until the algorithm converges to the point at which no set of directions can be found that results in a better value of an objective function, to within a preset tolerance.

### 3. RESULTS

For analysis of the optimization method's behavior during the registration process both above described deterministic optimization methods have been implemented and tested on medical datasets. Multiple test series with different intramodal and intermodal datasets have been conducted. For each trial a 2D-misregistration graph with the convergence track has been generated and the matching results visually inspected. In Fig. 2 one of the test dataset pairs has been shown. Other test datasets have been taken from the Visible Human Project dataset pool [5,6]. In this work we will use the MR and PET case to illustrate the observed, also in other trials, behavior of the tested objective functions and optimization methods. The sizes of the MR and PET datasets were  $256 \times 256 \times 55$  and  $128 \times 128 \times 31$  respectively. The registration procedures described in this article have been performed on a PC system (Athlon XP 3200+ 2.2 GHz, 512 MB RAM). The matching process using the mutual information measure and the Powell's optimization method took 2 min 42 sec (two-step multi-resolution approach) and required 2156 calculations of the mutual information objective function. In the second case (surface similarity measure and the Levenberg-Marquardt optimization method) the total running time took 3.7 sec (2.18 sec – pre-calculation of the Euclidean distance map and 1.52 sec – optimization). The optimal geometric transformations (see Fig. 2 (right)) obtained with these different methods were equal with respect to some preset tolerance. In Fig. 3 selected 2D misregistration graphs with the convergence track for the MR and

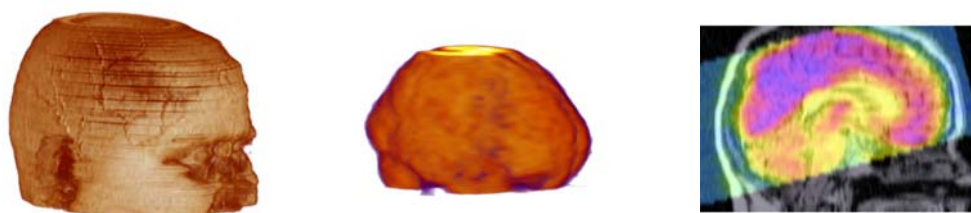


Fig.2. 3D view of the test data used in the optimization analysis: MR (left) and PET (middle) datasets of the same patient. Overlay view of the matched image volumes (right): the false color coded PET sagittal slice superposed onto the corresponding MR slice.

PET registration case have been presented. In the left column the surface similarity function landscapes for the selected pairs of search space principal axes have been shown. The black dots above the surfaces denote the single steps (or iterations) of the converging Levenberg-Marquardt optimization method. The equivalent misregistration graphs for the mutual information with the convergence tracks for the Powell's optimization method have been shown in the right column. The presented graphs reveal the characteristics of the objective function in the neighborhood of the

global optimum as well as the convergence behavior of both optimization methods in the analyzed registration problems. The gradient dependency and the direction sets of the analyzed search strategies can be easily observed in the presented graphs. Both optimization methods estimated successfully the optimal matching transformations in all of the tested cases and avoided falling into local minima. It was possible due to compatible initial positioning of the tested dataset pairs.

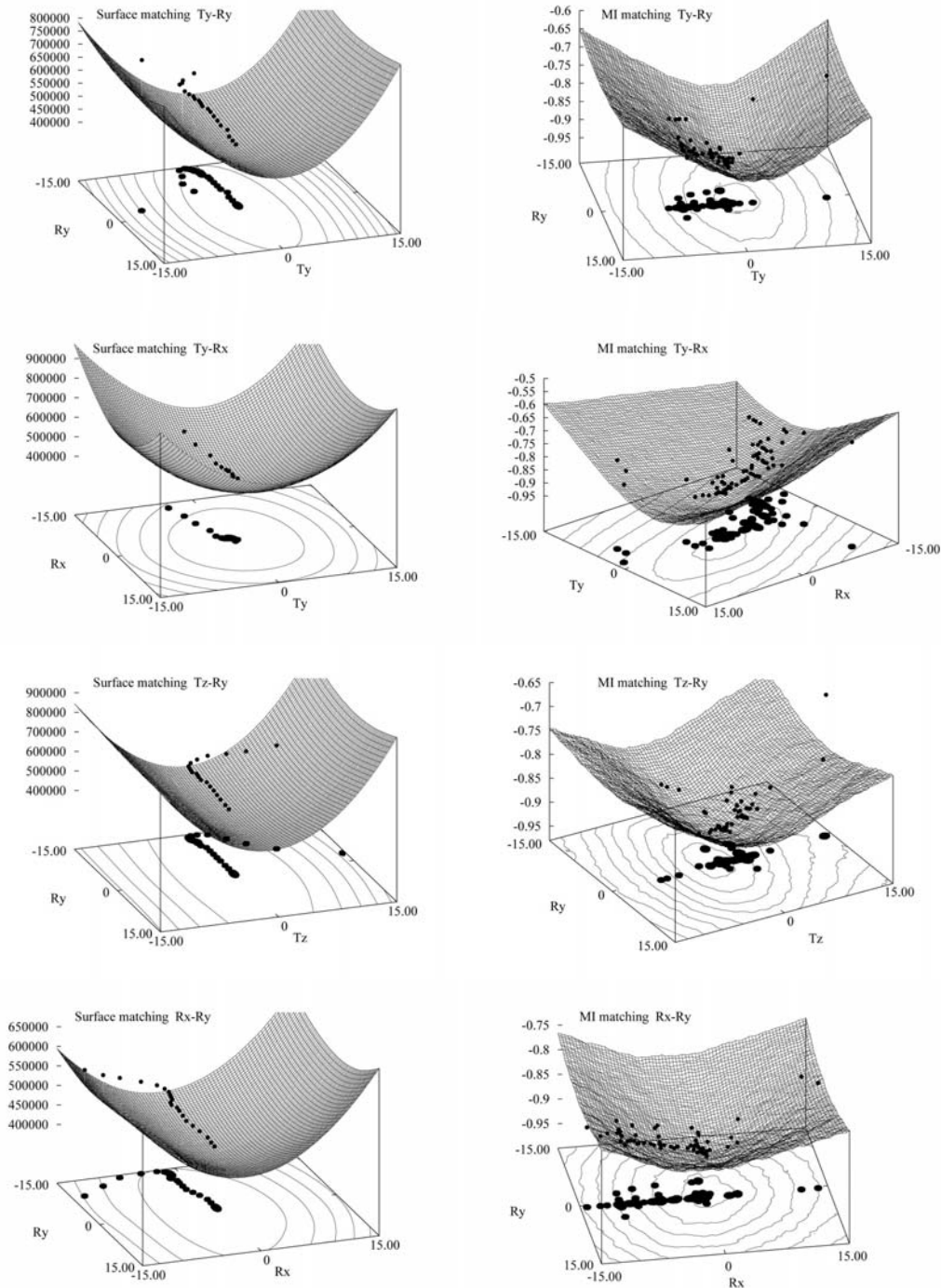


Fig.3. Selected 2D-misregistration graphs for the MR and PET test datasets. Left column: convergence behavior of the Levenberg-Marquardt method for the surface similarity measure. Right column: convergence behavior of the Powell method for mutual information similarity measure.



The presented above registration approaches together with robust segmentation techniques enable creation of highly detailed virtual patient-specific anatomical models (see Figures 1, 4 and 5), which provide the most efficient diagnostic assistance and can significantly improve many surgical or radiation therapy planning procedures. Variety of visualization methods enables different problem-oriented views of the whole model or the region of interest only. In Figures 4 and 5 different views of the same virtual model have been presented. Depending on the medical indications the virtual anatomical models can be visualized using 2D slice views or as 3D reconstructions. Effective exploration of the correlated datasets for diagnostic purposes can be achieved using inspection window or adjustable alpha-blending technique (see Fig. 5). For surgery or radiation therapy planning the surface rendering and volume rendering techniques (or both mixed with the 3D slice views) may be applied for effective visualization of the spatial relationships and to reveal some information that is not optimally visible in 2D (see Fig. 4). The most advanced approach to explore and interact with the virtual models offers the virtual reality environment, where the physician is fully or partially immersed in the virtual representation of the anatomical model.

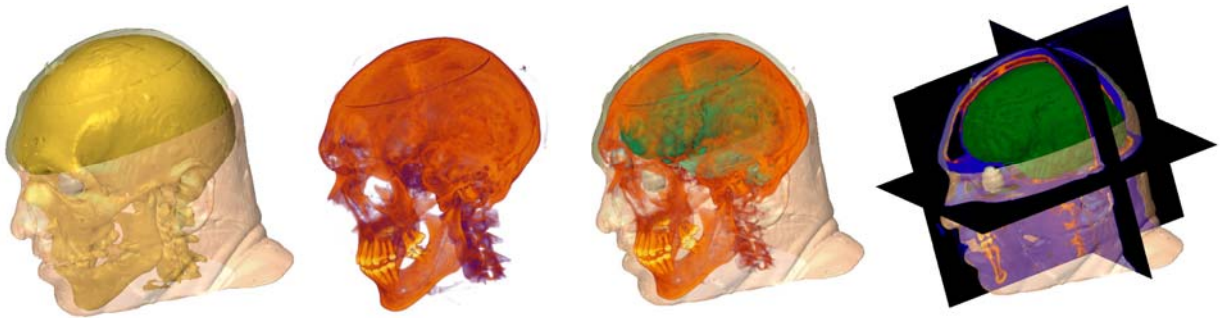


Fig.4. Three-dimensional visualization techniques: (from left) surface rendering, volume rendering, combination of volume and surface rendering, 3D-slices combined with surface rendering.

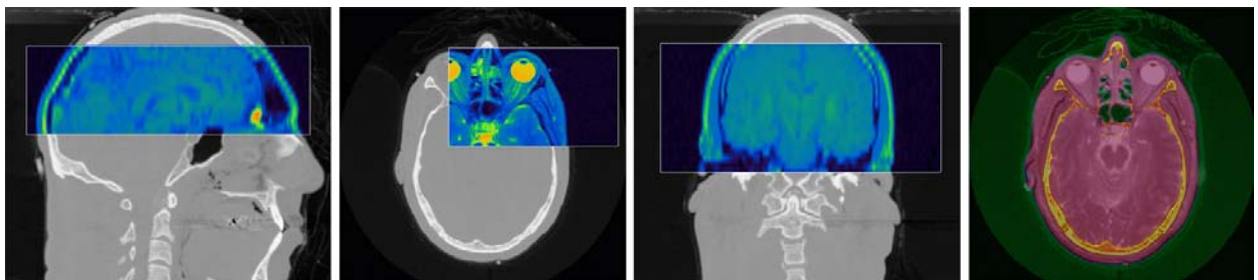


Fig.5. Two-dimensional visualization of registered volumetric datasets (CT and MR-T2): (from left) transversal, sagittal and coronal views with inspection window, transversal view of the semi-transparent MR dataset overlying CT volume.

#### 4. CONCLUSIONS

In this work different issues related to numerical methods in the registration of medical data have been presented and discussed. Two examples of different approaches to solve the optimization problem have been analyzed: the surface similarity measure optimized with the Levenberg-Marquardt method and the mutual information measure optimized with the Powell method. The two

deterministic optimization methods applied to different similarity measures reveal various convergence behavior and computational costs, but from the medical point of view both approaches result in the anatomically correct alignment. The correlated volumetric datasets found the base for the construction of the virtual patient-specific anatomical model. After the segmentation step the presented variety of visualization methods enables efficient exploration and utilization of the virtual patient model. In addition to the currently implemented optimization methods we plan in the future work to include also non-deterministic optimization methods like e.g. genetic algorithms or hybrid methods e.g. deterministic simulated annealing. Furthermore, we are working on the improvement of the rendering and model manipulation tools to achieve more intuitive and user-friendly interaction within the virtual scene. Further improvement of the multi-resolution approach and the code optimization will aim at the reduction of time required for the registration process.

### BIBLIOGRAPHY

- [1] NIKOLAIDIS N., PITAS I., 3-D Image Processing Algorithms, John Wiley & Sons, 2000.
- [2] HAJNAL J.H., HAWKES D.J., HILL D., Medical Image Registration, CRC Press, 2001.
- [3] PRESS W.H., FLANNERY B.P., TEUKOLSKY S.A., VETTERLING W.T., Numerical Recipes in C, Cambridge University Press, second edition, 1992.
- [4] MARQUARDT D.W., An Algorithm for Least-Squares Estimation of Nonlinear Parameters, Journal of the Society of Industrial and Applied Mathematics, Vol. 11, pp. 431-331, 1963.
- [5] SPITZER V., ACKERMAN M.J., SCHERZINGER A.L., WHITLOCK D., The Visible Human male: A technical report, Journal of the American Medical Informatics Association, Vol. 3, pp. 118-130, 1996.
- [6] National Library of Medicine, URL: <http://www.nlm.nih.gov/nlmhome.html>

We are very grateful to the *National Library of Medicine* [6] for the permission to work on and publish the Visible-Human-male datasets, and to Dr Derek Hill, UMDS, Guy's and St Thomas Hospitals, London, for the MR and PET datasets. This study has been partially supported by the Polish State Committee for Scientific Research (research project no. 7T11E01921).