ROTATED PRINCIPAL COMPONENTS FOR FUZZY SEGMENTATION SZINITIGGRAPHIC TIME SERIES IN INDIVIDUAL DOSE PLANING

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ABSTRACT
Time activity curves are assessed from whole body szintigraphic time series for individual dose estimation to limit the applicable therapeutic dose, preventing critical organs from substantial damage during radiation therapy. Whole body scans are projective images, thus organ ROIs may overlap. After careful image registration rotated principal components analysis is applied to the time series, identifying image parts with similar dynamics. This method allows the separation of overlapping structures providing fuzzy regions, where fractions of the pixel counts are assigned to the respective accumulating morphology. The summed counts from theses fuzzy regions are modified with the physical decay constant of the considered therapeutic isotope, providing the correct time samples for further dose calculation. Mono- or bi-exponential regression yields the time activity curves for the respective morphologies, passed to a standard dose calculation program. The newly developed method allows the fuzzy separation of overlapping structures in projective planar imaging series, yielding more accurate dose calculation in individual radiation therapy.

Keywords: factor analysis, image registration, dose planning, regression

1. INTRODUCTION

The internal application of radioactive elements for therapy has long tradition in oncology. The specific bindings of a radiopharmaceutical to tumor tissue or accumulation in glands are utilized to concentrate therapeutic dosage in the target region. But radioactive dose is not only focused there and collateral damage has to be generally avoided or minimized. For risk assessment of other organs, Monte-Carlo dose calculations for standardized phantom geometries are done. The effective dose per administered activity is calculated based on simple geometric modeling of the human morphology; there exist dose calculations for pediatric, female, pregnant, and male models. Results for all relevant body compartments are published in the ICRP reports. The principles are implemented in the software package MIRDOSE (Stabin 1996), the clinical standard until 2004, before OLINDA was deployed (Stabin and Siegel 2004).

With the further development of imaging modalities anthropomorphic models were further refined towards realistically shaped organs, segmented in 3D from real model 3D data sets.

Individual dose planning focuses on the assessment of pharmacokinetics and accumulation of the radioactive isotope in every single patient. Most therapeutic radiopharmaceuticals are mainly beta emitters and have no or only weak gamma lines in their emission spectra, thus assessment of the pharmaceutical local distribution is not possible. A common method is the use of an imaging isotope for assessment, i.e. an isotope with the same pharmacokinetics as the therapeutic isotope, but with sufficient gamma-emission to observe the metabolism of significant organs and the accumulation in lesions. The assessment of the organ specific time activity curves, the main information for the subsequent dose calculation, is based on the cumulative counts within the image regions, drawn manually on the whole body images, acquired at different points in time. To correct for the latter applied therapeutic isotope the summed counts are modified, reflecting the physical half-life-time of the therapeutic isotope (Mizarei et al 2013).

More recent approaches for individual dose planning are based on hybrid data SPECT-CT or PET-CT in combination with whole body data series for estimation of temporal evolution dose distribution (Lee 2014).

In the current approach specific tracer dynamics of metabolism, subject to dose calculation, is utilized to distinguish between organs and accumulating pathologies, even allowing the segregation of overlapping compartments. This method may potentially extract accurate dose information from simple whole body studies with its projective acquisition geometry. This information is only accessible from more costly 3D whole body tomographic studies.

2. MATERIALS

Time activity series from 6 patients were analyzed, four male and two female studies. Their age ranges from 53 to 72 years. After administration of 60 MBq In-111 whole body scans were acquired 20 min, 90 min, 24h, 48h, 72h, and 96 h after injection. Image data were acquired with a double headed gamma-camera system, Philips BrightView, the heads in 180 degree position. Anterior and posterior data stored in a 1024x512 image matrix, 2.8mm pixel-size and scan-speed 10cm/min.

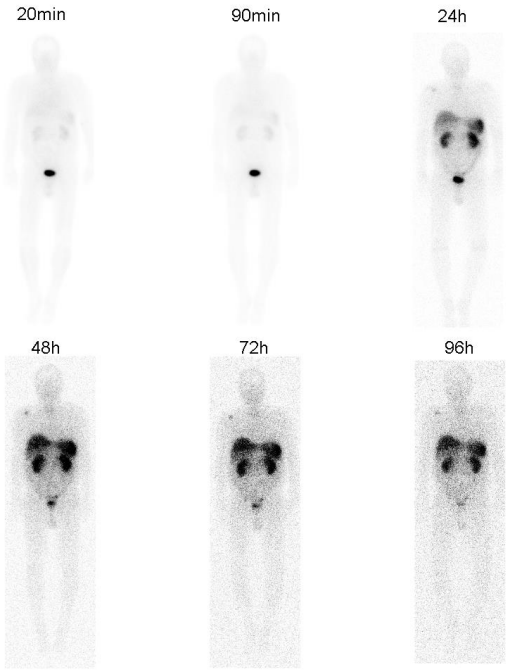

Figure 1: Anterior projection of the whole body time-activity study, i.e. six scans over a period of 96 hours. Projection images are acquired on a 1024 by 512 matrix, with 10cm/min scan speed. The intensity window is scaled to 45% of the maximum in each individual frame.

3. METHODS

Data analysis, i.e. dose assessment, comprises several steps, image registration, region drawing, factor analysis for automated separation of overlapping structures in projections, organ sampling and fitting of decay curves for each organ.

Each time activity series comprises 6 studies with simultaneously acquired anterior and posterior projections over a period of 96 hours, acquired in different scanning sessions. During each scan the patient-position may slightly differ, for meaningful data analysis careful image registration is required. Since the uptake and the subsequent decay of the radiopharmaceutical have locally different characteristics and organ specific visibility changes dramatically, a more sophisticated registration method is implemented. Surface oriented methods like chamfer matching are hardly applicable, since low contrast in late studies, i.e. 72 and 96 hours, allow no reliable extraction of outer body contours. It is aimed to utilize maximal available information provided by images, thus a pixel oriented approach is adapted for whole body image alignment.

Mutual information is a statistical measure from information theory; it describes the relation of symbols in two coherent data sets, respective tissues or morphologies. It is extensively used in image registration of multimodal data, where correlation methods are not applicable to modality specific manifestation of tissue. In perfectly registered images mutual information is maximized (Studholme et al. 1996, Hill et al. 1998, Crum et al. 2003).

For alignment of two-dimensional images the global maximum in a three-dimensional variable space, one rotational and two translational degrees of freedom, is determined. The solution space is searched with a steepest gradient algorithm, evaluating the mutual information equation

$$MI(X;Y) = \sum_{y \in Y} \sum_{x \in X} p(x,y) \log\left(\frac{p(x,y)}{p(x)\,p(y)} \right), \quad (1)$$

dependent on the joint probability $p(x,y)$ of images X and Y and the probabilities of both single images $p(x)$ and $p(y)$.

With the standard approach for dose assessment, regions are drawn manually over the essential organs and body parts, i.e. kidneys, liver, spleen, bladder, total body, background and reference. Typical regions are shown in Fig. 2.

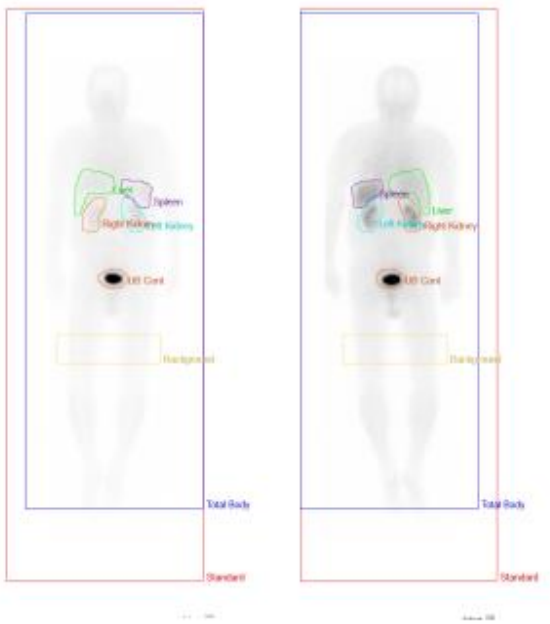

Figure 2: Manually drawn regions used in the standard approach for dose calculation. Regions may be drawn and displayed on, both, the anterior and posterior projection: kidneys (brown, cyan), liver (green), spleen (purple), bladder (ocher), body background (gold), total body (blue), and the reference standard (orange).

In many cases projections of kidneys overlap liver or spleen. A factor analysis approach was developed to separate those structures relying only on the projected images. Data from a rectangular region covering left and right kidney, liver and spleen are cut at each acquisition time, both from the anterior and posterior

image. Image sections are individually normalized to mean zero ($\mu=0$) and standard-deviation one ($\sigma=1$). ROI image data are reorganized from matrix to vector form and principal components analysis (PCA) is performed.

$$X = \begin{pmatrix} x_{11} & x_{12} & \cdots & x_{1m} \\ x_{21} & x_{22} & \cdots & x_{2m} \\ \vdots & \vdots & \ddots & \vdots \\ x_{N1} & x_{N2} & \cdots & x_{Nm} \end{pmatrix} \quad (2)$$

This is the normalized matrix of region of interest (ROI) image data. Each column contains the image data from a region, *m* is the number of analyzed ROIs and *N* is the number of pixels, each.

The correlation matrix *COR* is built

$$COR = X^T \cdot X, \quad (3)$$

and Eigenvectors C of the correlation matrix allow for decomposition of the image matrix X

$$X = I \cdot C^T + E, \quad (4)$$

Where *C* is a *p* by *m* matrix and *I* is a *p* by *N* matrix. The number of principal components *p* is assessed from the Eigenvalues, since the trace of the correlation matrix is the total variance of the data set, reflected by the sum of the Eigenvalues. Principal component images (PCI) are assessed by regression from image data and Eigenvectors. The context of time activity curves leads to the interpretation of the Eigenvalue matrix *C* as temporal evolution of radiopharmaceutical dynamics in accordingly to static morphological structures. These structures are represented by the PCIs and each observed image at each point in time is the weighted sum of these images, with the column of *C* associated with this time sample.

Principal components are not sufficient to reflect real physical properties of the analyzed regions; they are still orthogonal and provide an artificial decomposition of observed data. PCA itself explains the decomposition in terms of total variance and this is a proper unsupervised approach to separate noise from real dynamics in data. Neglecting the components higher than a certain threshold of cumulated Eigenvalues is a proper way to suppress the ambiguity component *E* from further analysis and leads to the number *p* of components

$$\sum_{i=1}^{p} \lambda_i \geq t, \quad (5)$$

where *t* is the desired fraction of the total variance, and λ_i are decreasingly sorted Eigenvalues.

To achieve accurate modelling of physiological processes, the arbitrariness of factorization is utilized

$$I \cdot C^T = IRR^{-1}C^T = F \cdot C^T, \quad (6)$$

where *R* is a *(p,p)* transformation matrix (*TT-1=1*). In principal components and factor analysis the matrices *F* and *C* represent the so called 'rotated' principal components, underlying certain optimization criteria, e.g. maximization of variance in Varimax rotation (Jackson 1991). In these transforms the components are kept mutually independent, i.e. the transformation matrix is orthonormal and its geometrical interpretation is a rotation. In our work we adapted that transform to oblique rotation, knowing a sufficient number of pixels of factor structures in advance, and then the transform matrix *R* can be estimated from

$$\begin{aligned} F_k &= I_k \cdot R \\ R &= (I_k^T I_k)^{-1} I_k^T F_k \end{aligned}, \quad (7)$$

where F_k is the part of the factor region known *a priori* and U_k is the respective amount of pixels in the PC images (Šámal et al 1987, 1989) .

In this approach the assumption of not totally overlapping structures leads to zero valued regions in the resulting factor images *F* providing the boundary condition for the transform matrix *R* (Backfrieder et al.1996).

The factor images provide fuzzy regions allowing the separation of overlapping organ structures in projection images of whole body scans. Based on this fuzzy segmentation more accurate time sampling of the organ specific tracer distribution is achieved. Summed counts are corrected for the decay constant of the therapeutic isotope and finally time activity curves for dose calculation are obtained by supervised mono- or bi-exponential regression of summed activities in the regions over time.

4. RESULTS

Registration of planar whole body projections in 2D provides accurate results. The images of the time series are registered to a single reference frame, generally the frame 90 minutes after injection, were all relevant morphologies are clearly manifested. An example for registration is shown with the linked display tool of the AnalyzeAVW software package (Biomedical Image

Resource, Mayo Clinic, Rochester, MN), cf. Figure 3. The reference (base) frame is displayed at the upper left, the matching frame on the bottom row; a weighted sum of both images is shown at the upper right. The tools allows for individual contrast enhancement of frames and provides a linked cursor to check accuracy.

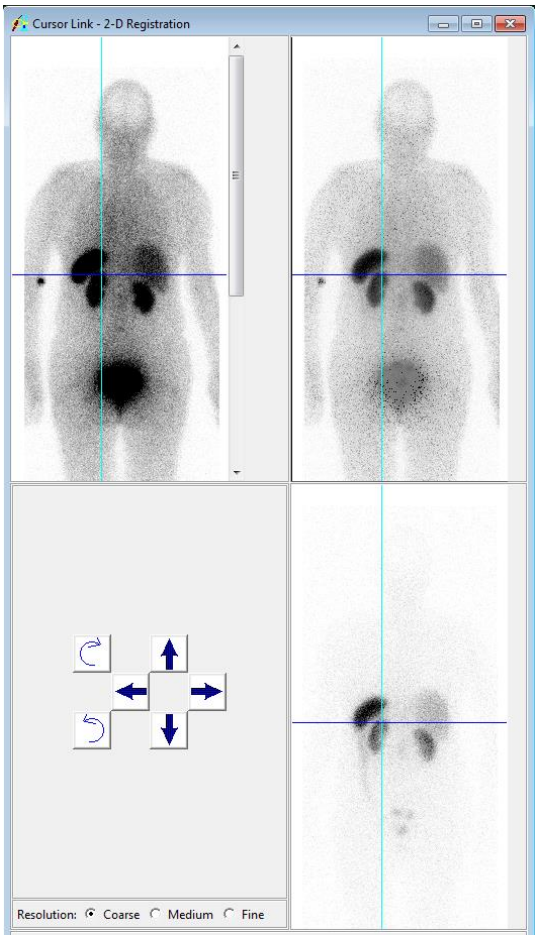

Figure 3: Cursor link tool for display of aligned images after mutual information registration. The upper left and the lower right image display the reference (base) frame and the matched frame. On the upper right a weighted overlay of both frames is shown. In this example tracer distributions 90 minutes (frame 2) and 48 hours (frame 4) after application are registered. The tool allows individual intensity scaling and weighting of each frame.

Separation of kidney and spleen was achieved by rotated principal components. The cumulated counts of all acquired projection image with overlapping regions is shown in Figure 4. The proper segmentation into a kidney region and a region containing the spleen with fuzzy parts in the overlapping area was accurately achieved, cf. Figure 5.

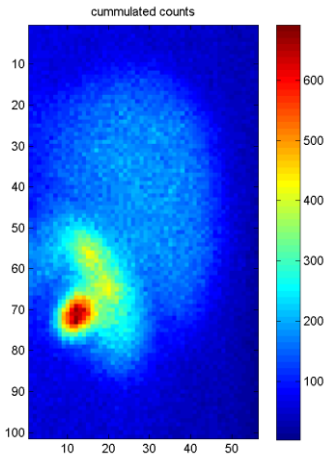

Figure 4: Cumulated counts of left kidney and spleen

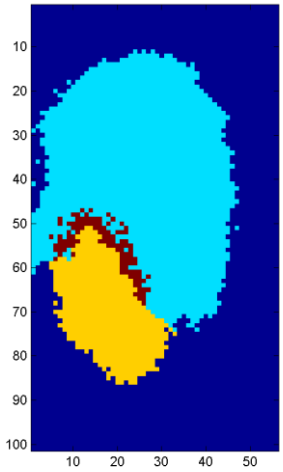

Figure 5: Overlapping regions calculated for liver and spleen. The kidney is marked ocher, the spleen is colored light blue, and areas belonging to both structures are marked dark brown.

5. DISCUSSION

The application of rotated principal components to time series for in vivo radioactive dose calculation allows the accurate segmentation of even overlapping structures in projection images. The method is an alternative to manual segmentation and an exploits whole available data, furthermore the application of an unsupervised method from multivariate statistics encourages to explore even non typical dynamic processes in time activity series. The rotation principle relies on *a priori* known parts of the image data, i.e. mutually non overlapping parts, where the respective structures are expected to be zero valued.

The method will be accurately tested with detailed mathematical phantom studies and a hybrid phantom, comprising known temporal tracer distribution and segmented morphologies from a 3D SPECT scan.

After careful clinical evaluation and comparison to results of standard whole body dosimetry, this method may be a further step toward accurate individual dosimetry based on organ specific time activity curves.

Even overlapping compartments may be accurately separated in the projective whole body scans. Alternatively this is only possible processing tomographic 3D image series, but low activity and long acquisition time are major drawbacks of these methods for use in dosimetry.

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Werner Backfrieder received his degree in technical physics at the Vienna University of Technology in 1992. Then he was with the Department of Biomedical Engineering and Physics of the Medical University of Vienna, where he reached a tenure position in 2002. Since 2002 he is with the University of Applied Sciences Upper Austria at the division of Biomedical Informatics. His research focus is on Medical Physics and Medical Image Processing in Nuclear Medicine and Radiology with emphasis to high performance computing. Recently research efforts are laid on virtual reality techniques in the context of surgical planning and navigation.

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