Distribution of Radiation in Synovectomy of the Knee with ^{166}Ho -FHMA Using Image Fusion

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ABSTRACT

Background: Radiation synovectomy is an effective technique for the treatment of chronic synovitis in patients with rheumatoid arthritis (RA), and is an alternative for surgical synovectomy. Holmium ferric hydroxide macroaggregates (^{166}Ho -FHMA) is suitable for radiation synovectomy, especially because it emits high-energy beta particles and a smaller proportion of low-energy photons that are suitable for gamma-camera imaging. **Objective:** The aim of this study was to develop a method to fuse ^{166}Ho -FHMA single photon emission computed tomography (SPECT) and magnetic resonance (MRI) images, to show the distribution of ^{166}Ho -FHMA inside the joint with images that localize synovitis. **Methods:** The knees of 6 patients with RA were treated with ^{166}Ho -FHMA. $^{99\text{m}}\text{Tc}$ -human immunoglobulin ($^{99\text{m}}\text{Tc}$ -HIG) SPECT images and MRI images were taken before ^{166}Ho -FHMA injections. ^{166}Ho -FHMA SPECT images were taken 4, 28, and 40 hours after injections. SPECT and MRI images were merged using a specific image fusion method, called mutual information algorithm, to study associations between anatomical and metabolic information from these images. **Results:** Fusion of SPECT and MRI images indicated that intensity of radioactivity was associated with the amount of synovitis. Activity distribution of ^{166}Ho -FHMA could be registered using anatomometabolic images. **Conclusions:** A new method to fuse the distribution of radiation in the synovectomy of the knee was developed using SPECT/MRI image registration. Image registration of SPECT and MRI can be used to determine the activity distribution of radioisotopes in relation to synovitis.

Key words: ^{166}Ho -FHMA, distribution, synovectomy, image fusion, SPECT

INTRODUCTION

Synovectomy by radioisotopes has been practiced in clinical rheumatology in several countries for over 50 years.¹⁻⁴ The most common target is a chronically inflamed knee joint of a

patient with rheumatoid arthritis (RA). Treatment of chronic synovitis using radiation synovectomy aims to control the inflammatory process that causes stiffness, pain, and severe structural damage to the joint. Radiation synovectomy has been developed as an alternative to surgical synovectomy.⁵ One radionuclide used today in radiation synovectomy is ^{166}Ho -ferric hydroxide macroaggregates (^{166}Ho -FHMA).⁶ ^{166}Ho -FHMA particles have two favorable properties that minimize radioactive leakage from the treated joint: a relatively short half-life of the radioisotope (26.8

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hours) and appropriate carrier size (3–12 μm). The other physical properties of ^{166}Ho -FHMA that make this radioisotope attractive for therapeutic application include a high energy β^-_{max} (1960 keV), and low-intensity, low-energy γ ray (80.57 keV; 6.2%) suitable for imaging. Single photon emission computed tomography (SPECT) studies indicate that most of the injected radiopharmaceuticals localize within the injected joint cavity.

A wide range of techniques for fusing of medical images has been developed in recent years. There are three general methods for fusing images from different image modalities: landmark matching, surface matching, and intensity matching, including mutual intensity information technique, which has been used for SPECT and magnetic resonance imaging (MRI) image fusion. Automated registration algorithm are mainly used for other anatomical organs than the knee, especially for the brain perfusion SPECT studies.⁷ However, automated registration algorithms and programs are useful and available for other organs.

High radioactivity of the knee joint cavity causes hot spots in the SPECT images. Therefore, distribution of radiation in the other parts of the knee joint is difficult to locate. As a consequence, the fusion of ^{166}Ho -FHMA SPECT images and MRI images is often inaccurate. To avoid this problem, we aimed to develop a method to facilitate the fusion of SPECT and MRI images to investigate the distribution of radiation in the knee using image fusion.

MATERIALS AND METHODS

Study subjects

The knee joints of 6 patients (4 female, 2 male) with RA were treated with ^{166}Ho -FHMA. Patients were immobilized and kept in bed for 3 days after ^{166}Ho -FHMA injection. Age of the patients ranged from 45 to 62 years, and the duration of disease ranged from 3 to 47 years (median, 14 years). All patients were treated with disease-modifying antirheumatic drugs, predominantly with methotrexate.

Radiopharmaceuticals

One week before treatment of the knee the patients were injected with Technescan[®] HIG la-

beled with $^{99\text{m}}\text{Tc}$, because HIG imaging offers a sensitive imaging method for the evaluation of synovial inflammatory activity. This modified polyclonal human immunoglobulin, in the amount of 1 mg (Technescan HIG, Mallinckrodt Diagnostica; Petten, Holland), was labeled with $^{99\text{m}}\text{Tc}$ pertechnetate, according to the instructions of the manufacturer. The patients were injected intravenously with 500–550 MBq $^{99\text{m}}\text{Tc}$ -HIG.

The knee joints were treated with intra-articular ^{166}Ho -FHMA injections (MAP Medical Technologies Oy; Tikkakoski, Finland). The treatment dose was 0.9–1.0 GBq of ^{166}Ho -FHMA.

SPECT imaging

Image acquisition was carried out with a ADAC Vertex + dual-head gamma camera (Philips Medical Systems, ADAC Laboratories, Milpitas). Imaging, starting 4 hours after injection, was performed by using a large field of view digital gamma camera, equipped with a low-energy, high-resolution collimator. Anterior and posterior whole-body scans, as well as anterior and lateral spot views of the knees, were obtained. SPECT images were taken. The total imaging time, including positioning, was 40 minutes.

All SPECT datasets consist of followed parameters: matrix size 128×128 , 32 projections per head acquired over 180 degrees, time per projection 15 seconds, pixel size 4.72 mm/pixel. SPECT images were acquired three times; first imaging was acquired 4 hours after ^{166}Ho -FHMA injection to the joint, second imaging 28 hours, and third imaging 40 hours after injection. SPECT images were acquired using the gamma energy of holmium (80 keV), with an average 19.8 ± 0.4 Mcounts ($\pm\text{SD}$) count statistics, with a range of 19.2–20.1 Mcounts. The first images were used as a reference to the effect of the distribution of holmium in the knee.

MRI imaging

The MRI images were taken using a SIEMENS Magnetom IMPACT Expert 1.0 T MRI Scanner (Siemens; Erlangen, Germany). Fat-suppressed T₁-weighted FLASH 3D images with gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA)-enhanced images were taken before radiosynovectomy. The knee was positioned neutrally and rotated in a transmit-receive flexible coil. MRI is a sensitive method to localize acute synovitis.

Pannus synovial hypertrophy and joint fluid are easily identified from these images. The MRI images were used as a standard reference to the fusion of the HIG images.

Data processing

SPECT images were reconstructed in HERMES image workstation (Hermes Medical Solutions; Stockholm, Sweden). SPECT images were reconstructed using the ordered subsets expectation maximization (OS-EM) iterative reconstruction algorithm, with 8 subsets and 6 iterations.⁸ Reconstructed slices were filtered by 3D image filtering; filter parameter for ¹⁶⁶Ho-FHMA SPECT images were Butterworth filter, cut-off frequency 1.6 cm⁻¹ and order 17.0, and for ^{99m}Tc-HIG SPECT cut-off frequency 1.0 cm⁻¹ and order 11.0.

Registration was performed with the application of MultiModality™ on HERMES using an automatic algorithm with 6 degrees of freedom (size changes were restricted, 3 for rotation and 3 for translation) and the Mutual Information method as a measure of similarity.⁹

Automatic registration was performed using the Minimization of Mutual Information algorithm,¹⁰ where second and third SPECT images were fused to the first SPECT images. In this registration technique, the statistical dependence between the image intensities of corresponding voxels in both image sets is defined, and it is assumed to be maximal if the images are geometrically aligned. The holmium distribution of the knee with isodose curves from the same-location region of interest (ROI) is possible by this method.

First fusion was made by fusing ^{99m}Tc-HIG SPECT images to the MRI images by automatic registration using Minimize Mutual Information. The second fusion was made by fusing ¹⁶⁶Ho-FHMA SPECT images to ^{99m}Tc-HIG SPECT images by the same method. The third fusion was made by registering semiautomatic ¹⁶⁶Ho-FHMA images to the MRI images by this same method.

Image fusion with a coregistered MR image was performed in order to correlate anatomical information with the image data obtained

through metabolic information by SPECT. Furthermore, the aim of the ^{99m}Tc -HIG study was to assess the efficacy of ^{99m}Tc -HIG scintigraphy to detect knee-joint inflammation by fusing it with MRI. The purpose was through the fusion of ^{99m}Tc -HIG to MRI to fuse ^{166}Ho -FHMA images to MRI images.

RESULTS

The ^{166}Ho -FHMA retains well in the joint cavity. The mean (SD) ^{166}Ho -FHMA total counts, scaled to the first-day average counts (100%) and time decay corrected were 98.0% (3.6%), with a range of 94.3%–103.4%, and, respectively, 82.9% (12.7%) on the third day with a range of 68.4%–95.5%.

A method to fuse the distribution of radiation in the synovectomy of the knee was developed using SPECT/MRI image registration. OS-EM increased the contrast of the images and improved separation between different regions.

Isodose curves (Fig. 1) of 90%, 70%, 50%, 30%, 10%, and 5% in different planes show the holmium activity distribution of the treated knee in SPECT images. The isodose curves associate with the amount of synovitis in the MRI images. ROI of inflamed synovium was marked semiautomatically on the MRI T1-weighted Gd-DTPA images. ROI of inflamed synovium fitted well with the SPECT images (Fig. 2).

DISCUSSION

Radiation synovectomy is an effective technique for the treatment of chronic synovitis in patients with RA. Although the treatment method has been used in many countries over decades, no fused knee images have been used to visualize the distribution of radiation. Reasons for this might include difficulties caused by a strong radioactivity of the knee-joint cavity.

We developed a new method to fuse high-radioactivity SPECT images and MRI images. This method offers the possibility to study the distribution of radiation inside the knee joint. Automated registration algorithms are mainly used for anatomical organs other than the knee, especially for the brain perfusion SPECT studies. However, automated registration algorithms or programs are useful and available for other organs, but visual observation is always important because the

automatic registration may fail. Thus, the results of the automated registration need to be validated by checking the goodness of fit.

High activity of the treated knee joint produces strong hot spots in SPECT images, causing difficulties to see the activity distribution in separate areas of the knee joint. The purpose of the SPECT imaging of the knee was to define the distribution of ^{166}Ho -FHMA inside the joint. The ^{99m}Tc -HIG SPECT imaging was done because of the localization the inflammatory focuses and at the same time for making ^{166}Ho -FHMA SPECT registration easier.

CONCLUSIONS

This study describes a method for the quantitative activity distribution of holmium in inflamed synovium using fused Gd-DTPA-enhanced MRI and SPECT images. In fused MRI images, isodose curves matched well with the inflamed synovium.

This fusion method offers the possibility to quantitate and calculate doses of radiopharmaceuticals in the knee. A reliable fusion method of SPECT and MRI images could be useful to document radiopharmaceutical distribution in the knee.

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