Post-Y90 Radioembolisation imaging with bremsstrahlung SPECT-CT and PET-CT

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Authors: S.-C. M. Wang, S. Evans, B. Camden, D. Farlow; Westmead, NSW/AU  
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Purpose

Yttrium-90 (Y90) is a radioisotope commonly used for therapeutic applications because of its beta particle emissions that enable high dose locoregional internal radiation therapy. Y90-labelled microsphere radioembolisation (RE) of the liver for treatment of unresectable primary and secondary liver malignancies is becoming an increasingly important therapy for patients who have failed or who are not suitable for alternative treatments, including surgery, chemotherapy (both systemic and arterial infusion), ablative therapies and chemoembolisation.

Y90-labelled resin microspheres (SIR-Spheres) and glass microspheres (TheraSpheres) are delivered intra-arterially to the liver via an angiographic catheter, acting as a flow-directed form of particle embolisation combined with brachytherapy. Y90 RE has been performed regularly at our centre since January 2009. One author (SCW) has extensive long-term experience of performing this procedure since 2000.

A longstanding difficulty with this treatment has been the inability to determine with precision a) the distribution of the Y90-particles after delivery, particularly to non-target tissues such as the bowel or the lungs, and b) the fraction of dose delivered to various tissues, in particular to intrahepatic tumours.

In mid-2009, Lhommel et al reported that positron emission of Y90 could be imaged using time-of-flight (TOF) positron emission tomography (PET) [1]. The decay of Y90 has a minor branch to the 0+ excited state [2], followed by internal positron/electron pair creation in 0.0032% of the administered dose [3]. We used this phenomenon to successfully image patients after Y90 RE with a conventional, non-TOF PET-CT scanner.

This poster has 2 key goals:

1. To demonstrate the feasibility, logistics and quality of imaging of the liver after RE with SIR-Spheres using a non-TOF PET-CT scanner, and comparing the studies to brehmsstrahlung gamma imaging using a SPECT-CT scanner in the same patients.
2. To qualitatively evaluate the distribution of delivered radiation to each patient's liver, liver tumours, lungs and other extrahepatic organs, in order to determine the safety of dose delivery as well as the risk of potential complications from nontarget radioembolisation.
Methods and Materials

10 patients with unresectable primary or secondary liver malignancy were treated by Y90 RE between January 2011 and November 2011, using SIR-Spheres (SIRTex Medical, Lane Cove, NSW Australia).

Patient characteristics are listed in detail in Table 1.

High resolution angiography was performed using a digital flat panel angiographic system (Allura, Philips Medical, Eindhoven, The Netherlands), using selective and superselective angiography as necessary to fully map the hepatic arterial supply, including depiction of all gastric, gastroduodenal and gallbladder artery branches. Superselective embolisation of specific branches was performed using fibred coils, depending on the vessels to be treated and the location of the branch origins.

CT hepatic angiography of the liver was performed in all patients with injection of dilute nonionic contrast agent into the hepatic arteries through one or more selective or superselectively placed catheters, according to the proposed arterial infusion points (Figures 4 to 7). Scans were obtained using a Toshiba Aquilion 16 multislice CT scanner. Following the CT, 100 MBq of Technetium-99m-macroaggregated albumin (99mTc-MAA) was injected into the hepatic circulation through the arterial catheters.

All patients were subsequently scanned using a conventional SPECT-CT scanner (Siemens Symbia, Siemens AG, Erlangen, Germany). Regions of interest were drawn over the lungs, liver and liver tumours to determine the relative uptake fractions of administered 99mTc-MAA (Figure 8).

Doses of Y90 SIR-Spheres from 0.8 to 3.0 GBq were given as detailed in Table 1. Except for one patient (J.M.), where the Body Surface Area method recommended by SIRTex Medical was used, doses were calculated using a volumetric modification of the partition model, based on CT volumetry of the liver regions and tumours to be treated, and tissue 99m-TcMAA counts. In general, target tissue exposure estimates were maintained within the following limits:

- Liver: $\leq 50$ Gy
- Tumour: $\geq 120$ Gy
- Lungs: $< 25$ Gy
Y90-labelled microspheres were delivered by slow intra-arterial infusion, if necessary through separately placed left and right hepatic arterial catheters using independent delivery systems with separately calibrated doses.

Imaging post-treatment was performed with both bremsstrahlung SPECT (Siemens Symbia SPECT-CT) and Y90 PET (first generation Siemens Biograph PET-CT).

Brehmsstrahlung SPECT acquisitions were performed as follows:

- Whole body, 64 projections at 35s per view
- High energy collimator, 66% window at 90keV
- CT for coregistration
- Attenuation correction was not performed

Y90 PET acquisitions were performed as follows:

- 10mins/bed, 3 positions
- Apex of lungs to below liver
- F-18 isotope selected
- Low dose noncontrast CT scan for attenuation correction and registration

Residual activities on catheters, lines and syringes were measured after dose delivery to determine actual injected activity.

As with pretreatment ROI segmentation of 99mTc-MAA scans, post-treatment ROI segmentation of Y90 PET-CT scans was performed to estimate the activity fraction delivered to each tissue. Exposure in Gray for each tissue was calculated using the formula:

\[
\text{Dose} = \text{Activity in tissue (Bq)} \times \text{Mean half-life of Y90 (332190.7 s)} \times \text{Exposure per emission (1.489x10^{-13} J/Bq s)} \ [4]
\]

A typical example is shown in Figures 9 and 10. This calculation was performed for 4 patients in this series.

SPECT and PET images were compared and correlated with diagnostic CT scans of the liver before and 3 months after treatment. Patients with extrahepatic abdominal nontarget dose deposition were treated with oral proton pump inhibitor (high-dose omeprazole) for 4 weeks.
Table 1: List of patient characteristics. Female-to-Male ratio = 1:1. HCC (hepatocellular carcinoma) 6/10, mCRC (Metastatic Colorectal Carcinoma) 3/10, mLS (Metastatic Leiomyosarcoma) 1/10. Mean age 72 years.

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Fig. 4: Patient W.A. Right hepatic angiogram during pretreatment workup. Note second arterial catheter placed in the left hepatic artery in preparation for separate left and right CT hepatic angiography and 99mTc-MAA infusions.

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Fig. 5: Patient W.A. Left hepatic angiogram prior to CTHA and 99m TC-MAA injection
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Fig. 6: Patient W.A. Right lobe CTHA via right hepatic arterial injection.

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Fig. 7: Patient W.A. Left lobe CTHA via left hepatic artery catheter.
**Fig. 8:** Patient W.A. Post-99mTc-MAA SPECT scans with ROIs drawn to segment the lungs, liver and tumours with relative count fractions tabulated below.

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Fig. 9: Patient W.A. Post-Y90 RE PET scans with ROIs drawn to segment the lungs, liver and tumours.

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Fig. 10: Patient W.A. Dose fractions and estimated dose delivered to each tissue calculated from the ROIs in Figure 6.
Results

For the 4 patients who had their relative tissue exposure fractions estimated, the estimates are listed in Table 2, which compares the tissue exposures calculated using the partition method with the exposures estimated using post-Y90 PET-CT. Lung exposures determined by Y90 PET-CT appeared to be higher, and liver exposures lower, than those estimated using the 99mTc-MAA scans.

Good quality bremsstrahlung and PET-CT scans were obtained in all patients. Y90 distribution could be reasonably accurately localised in all cases. Y90 was confirmed to be within the liver and target tumours in all patients.

A typical case showing the correlation between pre-treatment CTHA and 99mTcMAA SPECT, post-Y90 RE PET and brehmsstrahlung SPECT, and 3-month post-Y90 RE followup CT is shown in Figures 11 to 15.

Coregistration of PET-CT images appeared to be more consistent and robust than with SPECT-CT images. We found the PET images to be visually superior to bremsstrahlung images, with somewhat improved resolution, less artefactual "smearing", and more accurate coregistration with anatomic CT scans.

No patients developed nontarget RE complications subsequently. None required prophylactic treatment with omeprazole.

Satisfactory tumour control (tumour non-progression, necrosis or shrinkage) was obtained in all but one patient (L.B.), who developed rapid progression of his disease throughout the liver and extensive pulmonary metastatic disease within weeks of receiving Y90 RE therapy.
Table 2: Estimated tissue exposures for 4 patients. Apart from J.M., whose calculated dose was determined using the Body Surface Area method (SIRTex Medica), the exposures estimated using the modified partition method from 99mTc-MAA SPECT-CT scans are compared with those estimated from the post-Y90 PET-CT scans.

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**Fig. 11:** Patient D.S. Pretreatment coronal reformatted CTHA of the right lobe, showing extensive diffuse HCC growing into the main portal vein.

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Fig. 12: Patient D.S. 99mTc-MAA SPECT images in the coronal plane demonstrating tumour in both lobes, with the right lobe tumour showing good tracer uptake in the shape of an inverted pyramid, analogous to the CTHA appearance.

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**Fig. 13:** Patient D.S. Post Y90 PET-CT scan showing high isotope uptake in the treated right lobe tumour, extending into the main portal vein. The left lobe was not treated on this occasion.

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**Fig. 14:** Patient D.S. Corresponding post-Y90 RE brehmsstrahlung SPECT-CT scan showing high radioisotope uptake in the treated tumour. Note the less precise localisation of the radiation, and less accurate registration of the gamma image with the CT data.

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**Fig. 15:** Patient D.S. Post-Y90 RE followup CT scan at 3 months. The right lobe tumour has shrunk dramatically and no longer enhances on the arterial phase. The portal vein tumour thrombus has necrosed and has become a nonenhancing bland thrombus mass (arrow).

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Conclusion

High quality molecular imaging was obtained after Y90 RE with PET-CT with acceptable scan times, even when using a conventional non-TOF PET scanner.

Post-Y90 imaging, especially with fused PET-CT scans, can potentially exclude or detect nontarget radioembolisation. This in turn was used to determine whether patients required additional surveillance, or the routine administration of omeprazole. To date, we have found this to be a reliable means of predicting whether omeprazole is necessary after Y90 RE therapy.

The tissue exposures estimated from Y90 PET-CT scans for the 4 patients we have analysed differ from those derived from 99mTc-MAA scans, and require further research to determine the reasons for the differences.

The primary benefit of Y90 PET scans appears to be both improved visualisation of the actual delivered microspheres, and the potential to estimate the fractional dose delivered to each tissue. This may be helpful in assessing the risk of developing nontarget radioembolisation complications.

Our results suggest that conventional non-TOF PET-CT may be able to replace bremsstrahlung SPECT-CT to map the distribution of delivered radioactive microspheres after Y90 RE therapy.
References

Personal Information

S.C Wang\textsuperscript{1,2}, S. Evans\textsuperscript{3}, B. Camden\textsuperscript{3}, D. Farlow\textsuperscript{3}.

\textsuperscript{1}Discipline of Medical Imaging, University of Sydney

\textsuperscript{2}Department of Radiology, Westmead Hospital

\textsuperscript{3}Department of Nuclear Medicine and Ultrasound, Westmead Hospital

Hawkesbury Road, Westmead, Sydney, NSW 2145, Australia

\textbf{email:} shih-chang.wang@sydney.edu.au

\textbf{contact:} Prof. Shih-chang Wang, Department of Radiology, Westmead Hospital, Westmead NSW 2145 Australia