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First Author: Dr Yung H. KAO
Email: Yung.H.Kao@gmail.com

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State-of-the-art yttrium-90 selective internal radiation therapy: Technical aspects of artery-specific SPECT/CT partition model dosimetry

Yung Hsiang KAO (1), Andrew EH TAN (1), Richard HG LO (2), Kiang Hiong TAY (2), Mark C BURGMANS (2), Farah G IRANI (2), Li Ser KHOO (2), Bien Soo TAN (2), Pierce KH CHOW (3,4), David CE NG (1), Anthony SW GOH (1)
Departments of Nuclear Medicine and PET (1), Radiology (2) and General Surgery (3), SINGAPORE GENERAL HOSPITAL; Duke-NUS Graduate Medical School (4), SINGAPORE

Catheter-directed CT hepatic angiography + **^{99m}Tc-MAA SPECT/CT** + **Partition Modeling** = **Artery-specific SPECT/CT Partition model dosimetry**

INTRODUCTION

Radiation therapy for solid tumors is always effective when delivered at the right ***dose*** (Gy), in the right ***location***, to the right ***patient***, with the right ***intent***. Yttrium-90 (^{90}Y) radioembolization failure is invariably due to one or a combination of these four factors.

To date, radionuclide internal dosimetry for ^{90}Y radioembolization using ^{90}Y resin microspheres (SIR-Spheres®, Sirtex Medical Limited, Australia) has yet to embrace newer imaging modalities such as catheter-directed CT hepatic angiography (CTHA) and single photon emission computed tomography with integrated low-dose CT (SPECT/CT).

OVERVIEW OF DOSIMETRIC TECHNIQUE

The **artery-specific SPECT/CT partition model** is a dosimetric technique developed by our institution which integrates catheter-directed CTHA, technetium-99m-macroaggregated albumin (^{99m}Tc-MAA) SPECT/CT and partition modeling into a single unified state-of-the-art radiation planning technique for ^{90}Y radioembolization.

Catheter-directed CTHA accurately delineates the margins of perfused hepatic arterial territories, superior to digital subtraction angiography. **^{99m}Tc-MAA SPECT/CT** tomographically evaluates ^{99m}Tc-MAA hepatic biodistribution, superior to planar scintigraphy. **Partition modeling** is a validated and scientifically sound method of radionuclide internal dosimetry for ^{90}Y resin microspheres, superior to the body surface area method.

CLINICAL VALIDATION

From January to May 2011, 22 patients underwent ^{90}Y radioembolization using resin microspheres for inoperable hepatocellular carcinoma (HCC). Clinical outcomes of 10 patients planned by artery-specific SPECT/CT partition modeling were available for analyses.

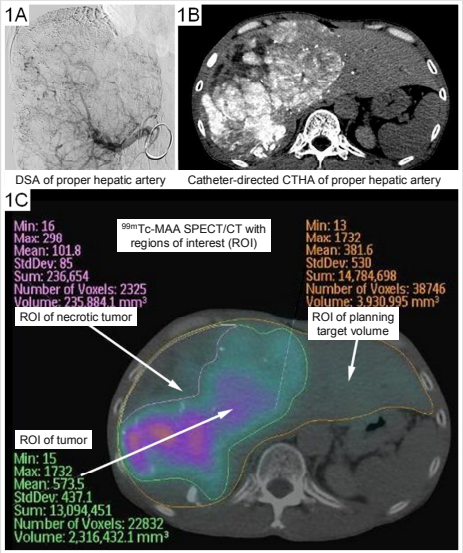
All 10 patients had no significant toxicities within 24 hours post-radioembolization. Follow-up data was available in 5 patients at the time of this report. Median biochemical and imaging follow-up were at 6.5 (range 4-11) and 8 (range 4-11) weeks respectively.

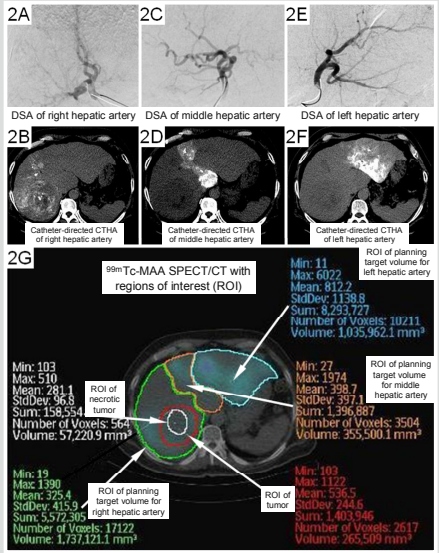
All 5 (100%) patients had size reduction of index lesions and no new lesions within planning target volumes. Serum alphafetoprotein was reduced by 87-95% in 2 patients. Clinical success was achieved in 80% (4 of 5 patients). Median survival has not yet been reached.

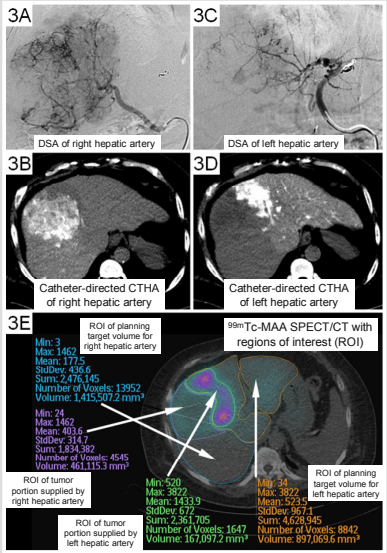
By partition modeling, a uniform tumor radiation dose of **80-90Gy** may be sufficient to achieve tumor size reduction at 4 weeks; **≥40Gy** to non-tumorous cirrhotic liver may cause liver function decline at 11 weeks; none developed pulmonary toxicity up to 7Gy to lungs.

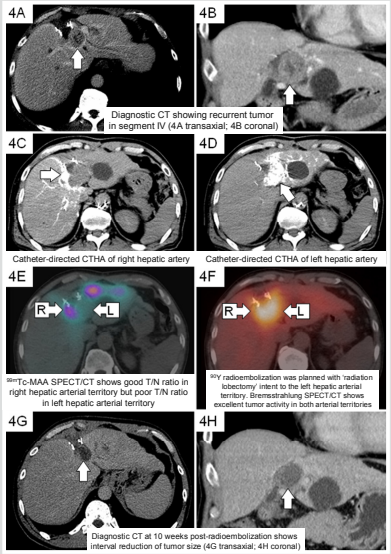
CONCLUSION

Early results show that artery-specific SPECT/CT partition modeling for state-of-the-art ^{90}Y radioembolization is safe and effective for inoperable HCC. Advanced clinical applications include **sub-lesional dosimetry**, precision **radiation segmentectomy/lobectomy** and the treatment of **hypovascular** tumors.









PRECISION DOSIMETRY FOR STATE-OF-THE-ART ^{90}Y RADIOEMBOLIZATION

SINGLE ARTERIAL TERRITORY

FIGURE 1A: Digital subtraction angiogram with catheter tip at the proper hepatic artery shows a large hypervascular tumor. **FIGURE 1B**: Corresponding catheter-directed CTHA shows the large enhancing hypervascular tumor and delineates arterial territory margins i.e. 'planning target volume'. Unenhancing tumor represents necrotic areas. ^{99m}Tc-MAA was injected at this location. **FIGURE 1C**: ^{99m}Tc-MAA SPECT/CT tomographically assesses ^{99m}Tc-MAA biodistribution and performs activity quantification. Visually guided by transaxial slices of the catheter-directed CTHA, ^{99m}Tc-MAA SPECT/CT regions of interest (ROI) are drawn for the planning target volume, tumor and necrotic areas. ROIs across all transaxial slices are interpolated into volumes of interest (VOI) to derive the SPECT counts and tissue volumes (cm^3). The artery-specific tumor-to-normal liver (T/N ratio) is calculated. Partition modeling derives the uniform radiation doses (Gy) and desired ^{90}Y activity. **(Download worked example 'SUPPLEMENTAL FIGURE 1' at our website)**

THREE ARTERIAL TERRITORIES

A liver with multifocal HCC is supplied by the right (**FIGURES 2A, 2B**), middle (**FIGURES 2C, 2D**) and left (**FIGURES 2E, 2F**) hepatic arteries. Volumes of interest (VOI) of the 3 planning target volumes on ^{99m}Tc-MAA SPECT/CT (**FIGURE 2G**) obtains **artery-specific** T/N ratios, liver-lung shunts, tumor and non-tumorous liver masses. Artery-specific partition modeling applied to each of the 3 planning target volumes obtains uniform radiation doses (Gy) to lung, tumor and non-tumorous liver compartments, which are unique to each arterial territory. The radiation therapy plan for each planning target volume is independent. The final radiation therapy plan is based on the physician's holistic assessment of patient-specific circumstances, in accordance to the desired clinical outcome, to achieve a personalized, accurate and scientifically sound radiation therapy plan for state-of-the-art ^{90}Y radioembolization. **(Download worked example 'SUPPLEMENTAL FIGURE 2' at our website)**

SUB-LESIONAL DOSIMETRY

'**Sub-lesional**' dosimetry is applicable for a tumor supplied by two or more arteries. Tumor parts supplied by different arteries may have different tumor-to-normal liver (T/N) ratios. Failure to take these variations into consideration during radiation planning can lead to clinical failure. **FIGURE 3** shows a single large HCC supplied by the right (**3A, 3B**) and left (**3C, 3D**) hepatic arteries. Regions of interest (ROI) on ^{99m}Tc-MAA SPECT/CT are in keeping with arterial margins delineated by catheter-directed CTHA, for sub-lesional dosimetry (**3E**). **(See worked example 'SUPPLEMENTAL FIGURE 3' at our website)**

RADIATION LOBECTOMY

Artery-specific radiation doses (Gy) to lung, tumor and non-tumorous liver are controlled by partition modeling. It is therefore possible to deliver any amount of radiation to a planning target volume, within limits of vascular stasis due to microparticle load. At sufficiently high radiation doses to cause significant injury to non-tumorous liver, the treatment intent may be considered as '**radiation segmentectomy/lobectomy**'. **FIGURE 4** shows a segment IV tumor supplied by the right and left hepatic arteries. ^{99m}Tc-MAA SPECT/CT shows poor T/N ratio of 1.4 (**4E**). ^{90}Y radioembolization by 'radiation lobectomy' was successful (**4G, 4H**).

Dosimetric worksheet and fully worked examples are available for download at: www.sgh.com.sg/Clinical-Departments-Centers/Nuclear-Medicine-PET