The Use of Hybrid Angio CT for SIRT

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Disclosure

- Proctor for Sirtex
- Research grant support from Sirtex
Selective Internal Radiation Therapy

- Selective delivery of yttrium-90 (Y\textsuperscript{90}) labelled microspheres via hepatic artery
  - High radiation dose to tumours (100 to 1000+ Gy)
  - Minimum dose to normal liver (< 50 to 70 Gy)
  - No dose to extra-hepatic organs
<table>
<thead>
<tr>
<th></th>
<th>Resin microspheres</th>
<th>Glass microspheres</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter</td>
<td>20 – 60 μm</td>
<td>2,500 Bq/sphere</td>
</tr>
<tr>
<td>Half-life</td>
<td>64.1 hrs (2.67 days)</td>
<td>1-2 million spheres per treatment</td>
</tr>
<tr>
<td>Mean beta energy</td>
<td>0.9367 MeV</td>
<td></td>
</tr>
<tr>
<td>mean penetration</td>
<td>2.5 mm</td>
<td></td>
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<tr>
<td>maximum range</td>
<td>11.0 mm</td>
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</tbody>
</table>

Resin microspheres:
- 50 Bq/sphere
- 40–60 million spheres per treatment

Glass microspheres:
- 2,500 Bq/sphere
- 1-2 million spheres per treatment

$^{90}$Y Labelled Microspheres

Y$^{90}$ Labelled Microspheres
Video Animation of SIR-Spheres® microspheres

Mode of Action
Overview of the SIRT Procedure

- **Step 1 : Work-up procedure**
  - Assess vascular anatomy
  - Injection of $^{99m}$Tc-MAA
  - Assess lung-shunt and Tumor:Normal liver ratio for dosimetry

- **Step 2 : Treatment (1–3 wks later)**
  - Prophylactic occlusion of extra-hepatic vessels (GDA, right gastric etc) to avoid non target embolisation to bowel
  - Administration of $^{90}$Y microspheres
  - Optional gamma camera scan to confirm implantation
Tc99 MAA Planar scintigraphy
Tc-99m MAA SPECT/CT
Liver to Lung Shunting

20%  74%
Infusion of Y-90 Microspheres

Prophylactic coil embo of GDA
Bremsstrahlung SPECT/CT Post SIRT
SIRT is Complex!

- SIRT is not TACE!
  - Vascular anatomy can be complex
  - Dosimetry calculation can be tricky
  - Potential for catastrophic complications
    - GI ulceration/bleeding
    - Radiation pneumonitis / dermatitis
- Careful planning and accurate delivery of an effective dose are critical for treatment success and prevention of complications
  - Close collaboration between IR and NM required
  - Hybrid Angio-CT invaluable tool
Side Effects

- Radiation pneumonitis
  - Ensure lung shunting < 20%, dose < 30 Gy
- Radiation induced liver disease (RILD)
  - Ensure dose to normal liver < 50 Gy
  - lower for cirrhotic liver
- Post embolisation syndrome
  - Much lower compared to TACE

(Lung shunting was 17%, 3.0 Gbq Y-90 infused)
Complications

- Non target embolisation
- GDA, gastric arteries
  - Radiation induced ulcers in stomach and duodenum
- Falciform artery
  - Radiation dermatitis over anterior abdominal wall
- Cystic artery
  - Acute cholecystitis
Anatomy is Challenging

- Hepatic and mesenteric vascular anatomy are complex and variable
- Altered vascular anatomy/collateral supply
  - prior surgical resection/TACE
- Extrahepatic supply of HCC
  - Parasitisation (especially large tumours)
- Meticulous angiographic technique mandatory to assess regional flow dynamics
Potential Extrahepatic Collaterals

Adrenal art

CD IA CTA

HC Kim et al. RadioGraphics 2005
Shiro Miyayama et al, CVIR 2006
Gastric and Falciform arteries originating from the Hepatic arteries

- Angiographic analysis in 250 patients

Song SY et al. JVIR 2006; 17:461-469
Gastric and Falciform arteries originating from the Hepatic arteries

- Angiographic analysis in 250 patients

Song SY et al. JVIR 2006; 17:461-469
Hybrid Angio-CT

- CT scan and Angio machine
  - in the same room sharing same table
  - can be used in combination or independently
• Easy to switch between Angio and CT
  – Move table
  – Self propelling CT on tracks

Helical CT with self propelling CT

Switch modality
Hybrid Angio CT (IVR-CT)

- Available in Japan since 1992
- Not many installations outside Japan
- Installed in SGH in October 2008
Advantages of Hybrid Angio-CT

- Ready availability of cross-sectional information
- Multi modality imaging options
  - CT ± fluoro ± DSA (± Ultrasound)
- Well suited for
  - Catheter directed intra-arterial CTA
  - Puncture under CT, manipulate under fluoro guidance
  - No need to transport the pat between angio and CT rms
- Improve operator confidence and patient safety, reduce procedure time and morbidity
Hybrid Angio CT at SGH

- Installed in October 2008
- 2247 procedures (Oct 08 – Mar 12)
  - CT guided procedures 931
  - Fluoro/Angio procedures 899
  - Hybrid procedures 417
- Interventional Oncology procedures
  - RFA 322
  - TACE 151
  - SIRT 129
Hybrid Angio-CT system enables catheter directed intra-arterial CTA of hepatic arteries without patient transfer
CT Liver

DSA

CD CTHA

CD CTHA
Right HA  
Left HA  
Collateral fr gastroepiploic
**DSA + CD IA CTA**

- Superior depiction of vascular anatomy
  - Tumour supply
  - Hepatic arterial anatomy
  - Aberrant extrahepatic collaterals (esp bowel)
- Accurate $^{90}$Y dose calculation
- Safe delivery of $^{90}$Y microspheres
**90Y Dosimetry**

- **Planning norms**
  - Target radiation dose to tumours: 120 Gy
  - Radiation dose limit to non-tumourous liver: 50-70 Gy
  - Radiation dose limit to lungs: 30 Gy

- **Methodology**
  - Empirical
  - Body surface area
  - Partition model*

Image-Guided Personalized Predictive Dosimetry by Artery-Specific SPECT/CT Partition Modeling for Safe and Effective $^{90}$Y Radioembolization

Yung Hsiang Kao$^1$, Andrew Eik Hock Tan$^1$, Mark Christiaan Burgmans$^2$, Farah Gillian Irani$^2$, Li Ser Khoo$^2$, Richard Hoau Gong Lo$^2$, Kiang Hiong Tay$^2$, Bien Soo Tan$^2$, Pierce Kah Hoe Chow$^{3,4}$, David Chee Eng Ng$^1$, and Anthony Soon What Goh$^1$

$^1$Department of Nuclear Medicine and PET, Singapore General Hospital, Singapore; $^2$Department of Diagnostic Radiology, Singapore General Hospital, Singapore; $^3$Department of General Surgery, Singapore General Hospital, Singapore; and $^4$Office of Clinical Sciences, Duke-NUS Graduate Medical School, Singapore

Compliance with radiobiologic principles of radionuclide internal dosimetry is fundamental to the success of $^{90}$Y radioembolization. The artery-specific SPECT/CT partition model is an image-guided personalized predictive dosimetric technique developed by our institution, integrating catheter-directed CT hepatic angiography (CTHA), $^{99m}$Tc-macroaggregated albumin SPECT/CT, and partition modeling for unified dosimetry. Catheter-directed CTHA accurately delineates planning target volumes. SPECT/CT tomographically evaluates $^{99m}$Tc-macroaggregated albumin hepatic biodistribution. The partition model is validated for $^{90}$Y resin microspheres based on MIRD macro-toxicities within 3 mo after radioembolization. The median time to best imaging response was 76 d (95% CI, 55–114 d). Median time to progression and overall survival were not reached. SPECT/CT-derived mean tumor-to-normal liver ratios varied widely across all planning target volumes (median, 5.4; 95% CI, 4.1–6.7), even within the same patient. Conclusion: Image-guided personalized predictive dosimetry by artery-specific SPECT/CT partition modeling achieves high clinical success rates for safe and effective $^{90}$Y radioembolization.

**Key Words:** $^{90}$Y radioembolization; $^{90}$Y selective internal radiation therapy; catheter-directed CT hepatic angiography; $^{99m}$Tc-macroaggregated albumin SPECT/CT; partition model MIRD
Prophylactic Coil Embolisation

- Radioembolisation Brachytherapy Oncology Consortium guidelines in 2006\(^1\)
  - recommended prophylactic coil embolisation of extrahepatic arteries to avoid extrahepatic deposition of Y90 spheres.
- Even with extensive coiling of extrahepatic collaterals, the rate of extrahepatic radiation injury was at least 4\(^{\%}\)\(^2\)

2. Gastrointestinal Ulcerations in 100 Consecutive Patients Treated with Y90 Microspheres: Rate and Associations JVIR (2008) 19:2 Supplement Pg S12-13
Accessory L gastric
Gastroduodenal art
Falciform artery

After coil embolisation
After coil embolisation
After coil embolisation
In most series, GDA and any suspicious bowel collaterals are coil embolised (up to 87%\(^3,4\)) and Y90 delivered from proper HA.

We minimise embolisation (23%) by:

- Splitting Y90 dose to deliver separately in left and right HA.
- CD IA CTHA performed before Y90 delivery to ensure no bowel enhancement.
Pre embo left CD CTHA

Embo coils

Post embo left CD CTHA
Radiation Dermatitis following Radioembolization for Hepatocellular Carcinoma: A Case for Prophylactic Embolization of a Patent Falciform Artery

Quor M. Leong, MBBS, MRCS, M.Med(Surgery), FRCSEd(Gen), Hee K. Lai, MBBch, MRCP(UK), Richard G.H. Lo, MBBS, FRCR, Terence K.B. Teo, MBBS, FRCR(UK), Anthony Goh, MD, MSc, and Pierce K.H. Chow, MD, PhD

Day 1 post-Y90 SIRT

Week 5 post-Y90 SIRT
• Retrospective review

• A patent FA was detected in 22 of 42 patients (52.3%).

• FA detection rates of DSA, CTHA and 99mTc-MAA SPECT/CT were 11.9%, 52.3% and 13.3% respectively (p<0.0001).

• An origin from the segment 4 artery was seen in 51.7% of HFAs.

Computed tomography hepatic arteriography has a hepatic falciform artery detection rate that is much higher than that of digital subtraction angiography and 99mTc-MAA SPECT/CT: Implications for planning 90Y radioembolization?

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b Department of Nuclear Medicine and PET, Singapore General Hospital, Outram Road, Singapore 169608, Singapore
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e Department of Surgical Oncology, National Cancer Center Singapore, 11 Hospital Drive, Singapore 168610, Singapore

ABSTRACT

Purpose: To compare the hepatic falciform artery (HFA) detection rates of digital subtraction angiography (DSA), computed tomography hepatic arteriography (CTHA) and 99mTc-macroaggregated albumin (99mTc-MAA) single photon emission computed tomography with integrated CT (SPECT/CT) and to correlate HFA patency with complication rates of yttrium-90 (90Y) radioembolization.

Material and methods: From August 2008 to November 2010, 79 patients (range 23–83 years, mean 62.3 years; 67 male) underwent pre-treatment DSA, CTHA and 99mTc-MAA scintigraphy (planar/SPECT/CT) to assess suitability for radioembolization with 90Y resin microspheres. Thirty-seven patients were excluded from the study, because CTHA was performed with a catheter position that did not result in opacification of the liver parenchyma adjacent to the falciform ligament. DSA, CTHA and 99mTc-MAA SPECT/CT images and medical records were retrospectively reviewed.

Results: A patent HFA was detected in 22 of 42 patients (52.3%). The HFA detection rates of DSA, CTHA and 99mTc-MAA SPECT/CT were 11.9%, 52.3% and 13.3%, respectively ($p < 0.0001$). An origin from the segment 4 artery was seen in 51.7% of HFAs. Prophylactic HFA coil-embolization prior to 90Y microspheres infusion was performed in 2 patients. Of the patients who underwent radioembolization with a patent HFA, none developed supra-umbilical radiation dermatitis. One patient experienced epigastric pain attributed to post-embolization syndrome and was managed conservatively.

Conclusion: The HFA detection rate of CTHA is superior to that of DSA and 99mTc-MAA SPECT/CT. Complications related to non-target radiation of the HFA vascular territory rarely occur, even in patients undergoing radioembolization with a patent HFA.
Fig. 2. Schematic drawings of the origin of the 29 HFAs detected in 22 patients: (a) origin from the segment 4 artery (S4) or MHA, (b) origin from the segment 3 artery (S3), (c) origin from a S3/S4 artery bifurcation, (d) origin from the bifurcation of the segment 2 artery (S2) and S3 near the umbilical point, and (e) origin from S2.
Prophylactic coil embo of falciform artery
Radioembolization with Infusion of Yttrium-90 Microspheres into a Right Inferior Phrenic Artery with Hepatic Tumor Supply Is Feasible and Safe

Mark Christiaan Burgmans, MD, Yung Hsiang Kao, MBBS, MRCP, FAMS, Farah Gillan Irani, MBBS, FRCR, FAMS, Erin Leslee Dames, MBBS, Terence Kiat Beng Teo, MBBS, FRCR, FAMS, Anthony Soon Whatt Goh, MBBS, MSc, FAMS, Pierce K.H. Chow, MBBS, PhD, MMed, FRSCE, FAMS, Kiang Hiong Tay, MBBS, FRCR, FAMS, and Richard Hoau Gong Lo, MBBS, MMed, FRCR

ABSTRACT

Purpose: To evaluate the feasibility and safety of yttrium-90 (90Y) radioembolization through the inferior phrenic arteries (IPAs).

Materials and Methods: Retrospective analysis of 108 patients referred for radioembolization to treat primary (n = 103) or secondary (n = 5) liver malignancy was performed. Five patients had malignant hepatic tumors supplied by the IPA and met criteria for infusion of 90Y spheres into the IPA. Digital subtraction angiography (DSA), catheter-directed computed tomographic (CT) angiography, and technetium-99m (99mTc) macroaggregated albumin (MAA) single photon emission CT (SPECT)/CT were used to plan treatment. Bremssstrahlung SPECT/CT was performed 1 day after radioembolization. Follow-up included clinical and biochemical tests and cross-sectional CT or magnetic resonance imaging.

Results: Parasitized extrahepatic arteries were detected in 37% of patients (n = 40). Of these, 62.5% (n = 25) had tumor supply through an IPA. Of the patients with IPA supply, 20% (n = 5) underwent infusion of 90Y into the right IPA. Reasons for disqualifying patients from infusion into the IPA were less than 10% tumor supply (n = 11), failed catheterization of IPA (n = 3), arterioprtovenous shunt (n = 2), failed identification of IPA on pretreatment angiography (n = 1), and gastric or esophageal enhancement on catheter-directed CT angiography (n = 3). In all five patients, technical success was demonstrated on 90Y imaging, with no significant extrahepatic radionuclide activity. No adverse events related to IPA radioembolization occurred at mean follow-up of 4.5 months (range, 2.2–10.1 mo).

Conclusions: Delivery of 90Y microspheres through the right IPA is feasible and safe with the use of catheter-directed CT angiography in addition to DSA and 99mTc MAA SPECT/CT in patients with tumors with greater than 10% IPA supply.
Infusion of Y-90 Microspheres into Inferior Phrenic Artery is Safe

JVIR 2012 Oct;23(10):1294-1301
SIRT for HCC – SGH Experience

- Jan 2008 – Jun 2012
- 103 patients (non trial)
  - 47.6% Hep B, 23.3% Hep C
- Median Overall Survival (OS) 14.4 mths
  - BCLC B 23.8 mths
  - BCLC C 13.6 mths
  - PV thrombosis 11.0 mths
  - No PV thrombosis 18.1 mths
Median survival:
BCLC B: 23.8 months
BCLC C: 13.6 months
P = 0.048 (Log-rank test)
Y-90 SIRT of HCC: Overall Survival by BCLC Stage

Salem et al. Gastroenterology 2010

Sangro B et al. Hepatology 2011
SIRT for HCC – SGH Experience

- Overall disease control rate 64.7% (RECIST)
- Target lesion response rate 98.3%
- Progression of disease mainly due to new lesions (69.2%)
- Survival outcome comparable to western populations
  - BCLC B: Salem 17.2, Sangro 16.9, SGH 23.8 months
  - BCLC C: Salem 7.3, Sangro 10.0, SGH 13.6 months

Salem et al. Gastroenterology 2010
Sangro B et al. Hepatology 2011
ASCO 2013 abstract #114364
Multicenter Phase II Study of Sequential Radioembolization-Sorafenib Therapy for Inoperable Hepatocellular Carcinoma

Pierce K. H. Chow1,2,3*, Donald Y. H. Poon2, Maung-Win Khin4, Harjit Singh5, Ho-Seong Han6, Anthony S. W. Goh1, Su-Pin Choo2, Hee-Kit Lai1, Richard H. G. Lo1, Kiang-Hiong Tay1, Teong-Guan Lim1, Mihir Gandhi3,7, Say-Beng Tan3,7, Khee-Chee Soo1,2,3, for the Asia-Pacific Hepatocellular Carcinoma Trials Group

1 National Cancer Centre, Singapore, Singapore, 2 Singapore General Hospital, Singapore, Singapore, 3 Duke-NUS Graduate Medical School, Singapore, Singapore, 4 Yangon Gastrointestinal and Liver Centre, Yangon, Myanmar, 5 Selayang Hospital, Selangor, Malaysia, 6 Seoul National University Bundang Hospital, Bundang, South Korea, 7 Singapore Clinical Research Institute, Singapore, Singapore

Abstract

Background: The safety and tolerability of sequential radioembolization-sorafenib therapy is unknown. An open-label, single arm, investigator-initiated Phase II study (NCT0071279) was conducted at four Asia-Pacific centers to evaluate the safety and efficacy of sequential radioembolization-sorafenib in patients with hepatocellular carcinoma (HCC) not amenable to curative therapies.

Methods: Sorafenib (400 mg twice-daily) was initiated 14 days post-radioembolization with yttrium-90 (90Y) resin microspheres given as a single procedure. The primary endpoints were safety and tolerability and best overall response rate (ORR) using RECIST v1.0. Secondary endpoints included: disease control rate (complete [CR] plus partial responses [PR] and stable disease [SD]) and overall survival (OS).

Results: Twenty-nine patients with Barcelona Clinic Liver Cancer (BCLC) stage B (38%) or C (62%) HCC received a median of 3.0 GBq (interquartile range, 1.0) 90Y-microspheres followed by sorafenib (median dose/day, 600.0 mg; median duration, 4.1 months). Twenty-eight patients experienced ≥1 toxicity; 15 (52%) grade ≥3. Best ORR was 25%, including 2 (7%) CR and 5 (18%) PR, and 15 (54%) SD. Disease control was 100% and 65% in BCLC stage B and C, respectively. Two patients (7%) had sufficient response to enable radical therapy. Median survivals for BCLC stage B and C were 20.3 and 8.6 months, respectively.

Conclusions: This study shows the potential efficacy and manageable toxicity of sequential radioembolization-sorafenib.

Trial Registration: ClinicalTrials.gov NCT00712790.


Editor: Gianluigi Giannelli, University of Bari Medical School, Italy.
## Primary Liver Cancer

<table>
<thead>
<tr>
<th>Title</th>
<th>Setting</th>
<th>Sponsor</th>
<th>Study ID</th>
<th>Treatment Arm(s)</th>
<th>Location</th>
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</thead>
</table>
Study to compare selective internal radiation therapy (SIRT) versus sorafenib in locally advanced hepatocellular carcinoma | Hepatocellular Carcinoma | Collaborative Group Study | NCT01135056 | Sorafenib *versus* SIR-Spheres microspheres | Asia-Pacific |
| SARAH  
Sorafenib versus radioembolization in advanced hepatocellular carcinoma | Hepatocellular Carcinoma | Collaborative Group Study | NCT01482442 | Sorafenib *versus* SIR-Spheres microspheres | France |
| SORAMIC [www.soramic.de](http://www.soramic.de)  
Sorafenib and micro-therapy guided by primovist-enhanced MRI in patients with inoperable liver cancer | Hepatocellular Carcinoma | Investigator-Initiated Research Trial | NCT01126645 | Sorafenib *versus* SIR-Spheres microspheres > Sorafenib | Europe |
| CHOLANGIOSIR  
Second-line therapy of unresectable cholangiocarcinoma by radioembolization | Intra-Hepatic Cholangiocarcinoma | Investigator-Initiated Research Trial | NCT01383746 | SIR-Spheres microspheres | France |
Hybrid Angio – CT in SIRT

- Superior depiction of vascular anatomy
  - Tumour supply
  - Hepatic arterial anatomy
  - Aberrant bowel collaterals
- Safety and accuracy of $^{90}$Y delivery enhanced
  - Personalised dosimetry
  - Decrease need for prophylactic embolisation
- Improve operator confidence and reduce procedure time
  - Decrease morbidity and enhance patient safety
Thank you for your attention!