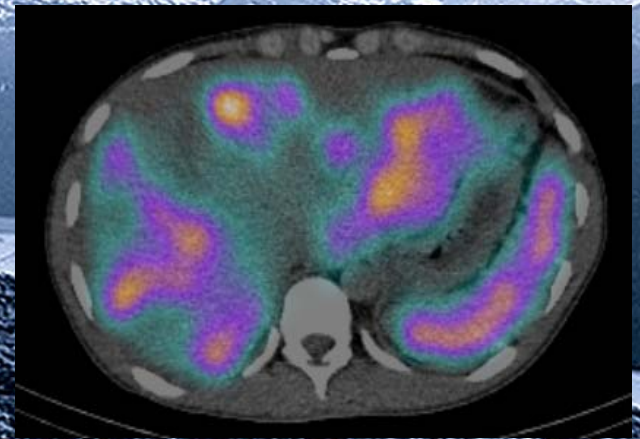
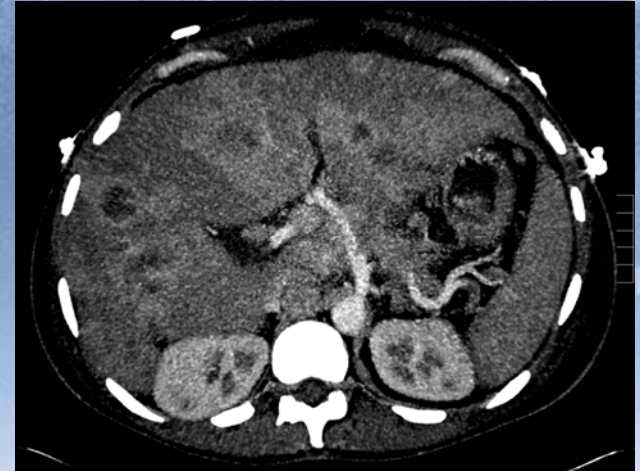


CIRA Case of the Week

February 2016



Case Courtesy of Dr. Edmund Ng
University of British Columbia



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Clinical Presentation

BW is a previously healthy 26 year old expectant father whose wife is 4 months pregnant

He presents to hospital July 2014 with 3 month history of

- fatigue
- weight loss
- night sweats
- vomiting
- early satiety
- irritable bowel (diarrhea and constipation)



Imaging Findings

Work up with ultrasound and CT July 28, 2014 demonstrates multiple liver lesions suspicious for metastasis.



A liver biopsy was completed (result withheld)

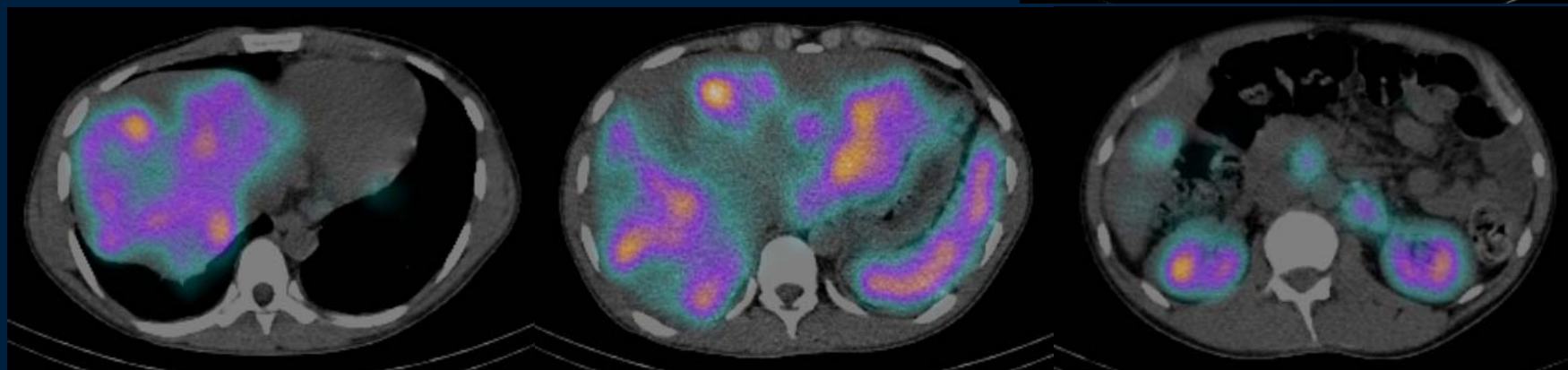
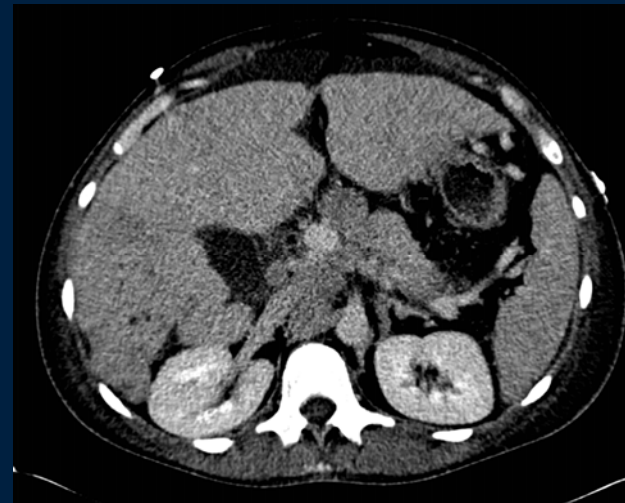


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Additional Imaging

Chest CT from Sept 18, 2014 - negative
CT of the abdomen demonstrated
progressive metastatic disease in the liver.
Pancreatic lesion was also identified.



Extensive octreotide avid metastatic disease within the liver and multiple abdominal lymph nodes



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Clinical Presentation and Labwork

BW was readmitted to hospital Oct 30, 2014, when he developed increasing confusion, night sweats, rigors and shakes consistent with hypoglycemia

urine 5-HIAA: 3651

Chromogranin A: 3060

C-peptide: 2944

Blood Glucose [lowest 2.9] requiring
D5W infusion



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Pathology

Liver biopsy completed Aug 2,
2014 was consistent with

**well differentiated
metastatic neuroendocrine
tumour, likely metastatic**

- Mitosis 0 / 50 on high power field
- Ki 67 < 5%



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Patient Treatment Plan

- BW started systemic chemotherapy with temozolomide and capecitabine (Nov 5 - 19th for 14 days)
- Growth hormone therapy (to increase insulin resistance)
- **Diazoxide** (Nov 6-8th, for 3 days, discontinued due to edema)
- **Octreotide** (pre admission as well as from Nov 24th onwards)
- Corn starch
- **glucagon infusion**
- **Continuous D5W, D10W infusion** with hourly glucometer assessments
- developed issues with hyponatremia and **transferred to ICU for monitoring**
- discussion of possible **surgical debulking** vs **yttrium 90 embolization** of liver metastasis



Y90 Mapping

Lab:

Imaging:

Pretreatment angiography:

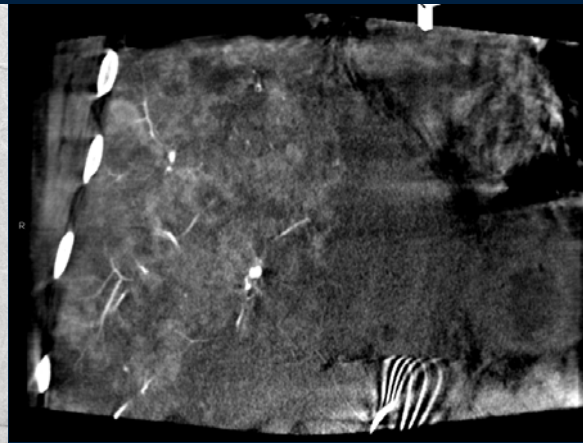
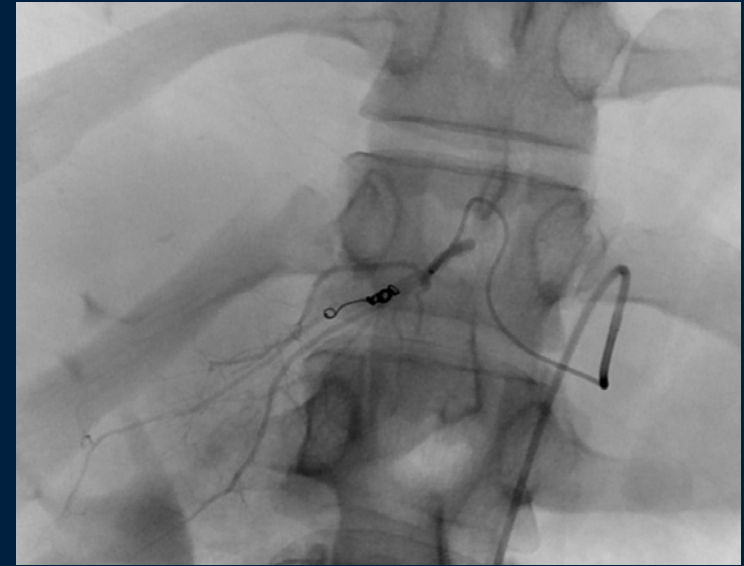
Shunt fraction analysis:

Administration:

Confirmation of delivery:

Follow up

Segment 4a artery arising from the left hepatic artery. This was embolized using pushable coils for redistribution



A DSA and Dyna CT confirmed appropriate right hepatic lobe administration site.

Technetium MAA was administered in the replaced right hepatic artery.



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Shunt Analysis

Lab:

Imaging:

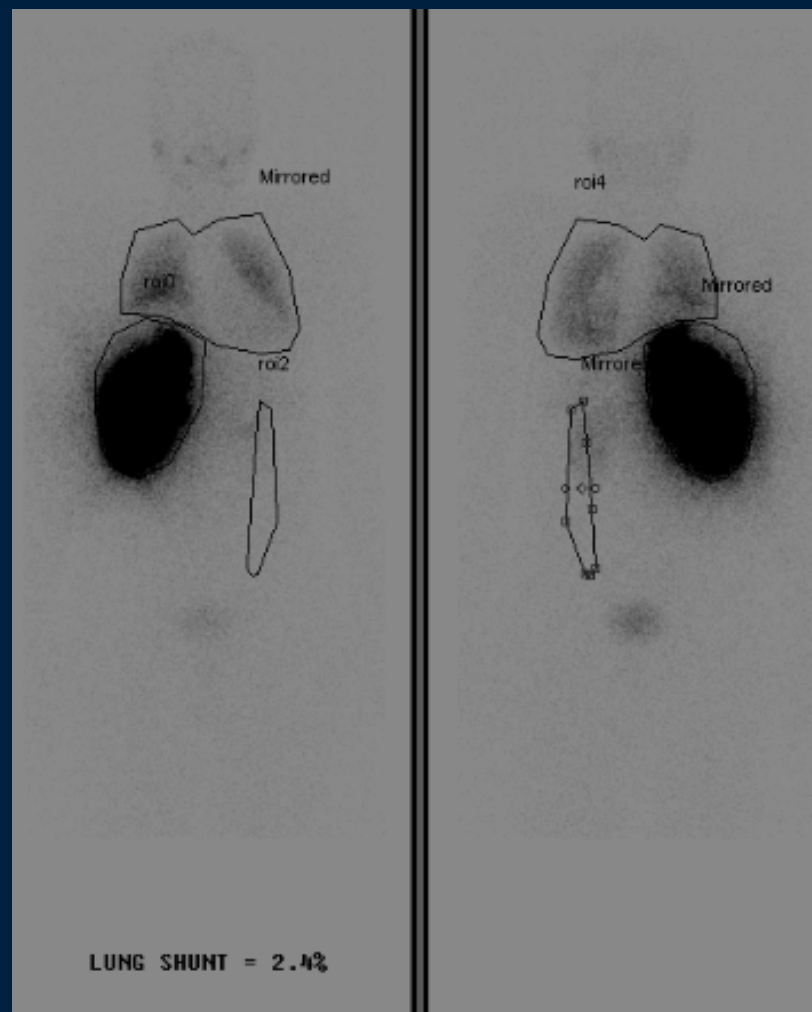
Pretreatment
angiography:

Shunt fraction
analysis:

Administration:

Confirmation of
delivery:

Follow up



A low lung shunt fraction (2%) enables Mr. BW to undergo Y90 administration.



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Y90 Administration

Lab:

Imaging:

Pretreatment angiography:

Shunt fraction analysis:

Administration:

Confirmation of delivery:

Follow up:

Special approval was provided from Health Canada to administer an unused dose of Y90 microspheres



BW was compatible for right lobe administration from an unused 3.1 GBq dose of SIRsphere beads, leftover from a previous patient due to an unexpected celiac artery dissection.

3.1 GBq of SIRspheres administered into replaced right hepatic artery



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Post Y90 Bremsstrahlung Scan

Lab:

Imaging:

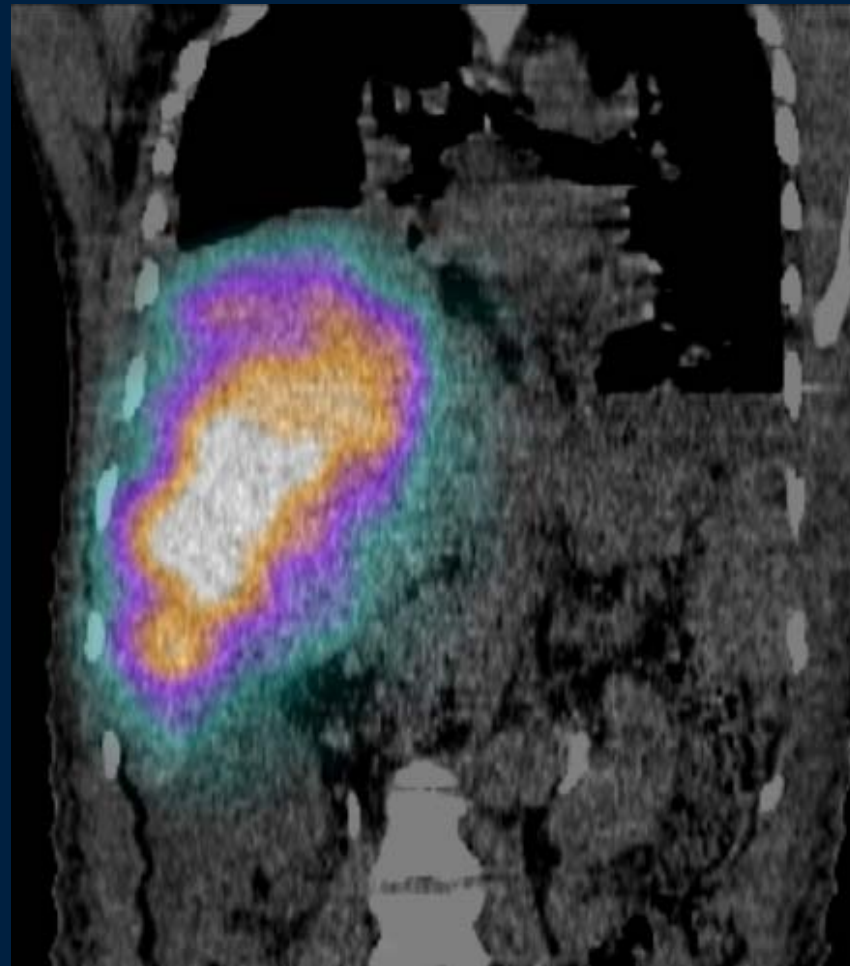
Pretreatment
angiography:

Shunt fraction
analysis:

Administration:

Confirmation of
delivery:

Follow up



A bremsstrahlung radiation scan performed approximately 1 hr post administration demonstrated diffuse activity within the right lobe of the liver

No extrahepatic intra-abdominal embolized activity is identified.



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Patient Outcome

Lab:

Imaging:

Pretreatment angiography:

Shunt fraction analysis:

Administration:

Confirmation of delivery:

Follow up

Mr. BW was **discharged** from hospital Dec 11, 2014

No carcinoid crisis post treatment

Titrated off D10W infusion with stable blood glucose of 6-8 and no hypoglycemic episodes

Titrated off octreotide infusion

Started on ursodial for hepatoprotection

Epilogue: He was present for the birth of his baby girl. During that time, Mr. BW did not suffer from hypoglycemic episodes. Mr. BW subsequently had a left sided administration. He is currently on Everolimus.



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Insulinoma

- most common pancreatic neuroendocrine tumor (55%), deriving from pancreatic islet cells, that secretes insulin
- About 90% benign and **10% malignant** (metastases are present)
- Approximately 10% of patients have multiple insulinomas;
 - of patients with multiple insulinomas, 50% have (MEN1)
- Malignant tumors are usually larger (average size 6.2 cm), and a third of them have metastasized to the liver.
- Tumor secretes insulin in short bursts, causing fluctuations in blood levels



Selective Internal Radiation Therapy (Y90) Technique

Lab:	assess hepatic and renal function, establish baseline tumor markers
Imaging:	A 3-dimensional (3D) CT volumetric analysis to calculate tumor volume, total liver volume, and liver reserve. This will estimate the required administered dose.
Pretreatment angiography:	hepatic angiography (pre-SIRT mapping procedure) 1 to 3 weeks before the treatment for dosimetry calculations and embolization to prevent non targeted embolization and encourage hepatic redistribution
Shunt fraction analysis:	hepatopulmonary shunt is assessed using ^{99m} Tc macroaggregated albumin (MAA) to avoid extrahepatic toxicity (e.g. radiation pneumonitis)
Administration:	hepatic arteriogram with targeted delivery of beads to liver lobe/segments
Confirmation of delivery:	nuclear medicine study: Bremsstrahlung Scan
Follow up	CT at 3 and 6 months to assess response



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Yttrium 90 for Treatment of Diffuse Liver Metastasis

Table 3

A summary of major studies of SIRT in treatment of NETLM

Investigator	N	Treatment	Overall Response Rate (%)	Survival
SIRT in mixed cohort in chemorefractory NETLM				
Kennedy	148	SIRT	86	70 mo
King	34	SIRT + 5-FU	64.7 (symptomatic relief = 55%)	35 mo
Saxena	48	SIRT + 5-FU	77	35 mo
Cao	58	SIRT + 5-FU	66	36 mo
Rhee	42	SIRT	94	28 mo
Jakobs	25	SIRT	96 (symptomatic relief = 92%)	96% (1 y)
Coldwell	84	SIRT	100 (symptomatic relief = 80%)	NR
Ezziddin	23	SIRT	91 (symptomatic relief = 80%)	29 mo
Paprottka	42	SIRT	97 (symptomatic relief = 95%)	95% (16 mo)



Conclusion

- Y90 microspheres is a safe and effective treatment option in patients with unresectable neuroendocrine tumours with hepatic metastasis.
- This case demonstrates the utility of transarterial radioembolization in the symptomatic treatment of malignant insulinoma.



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