



THE **HOLMIUM PLATFORM**

Three integrated products
DELIVERING INDIVIDUALIZED SIRT
at its full potential



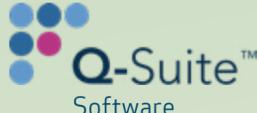
from **ACCESS**
to **CLOSURE**
INTERVENTIONAL
ONCOLOGY



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THE HOLMIUM PLATFORM



The Holmium Platform delivers a first in SIRT; a comprehensive end-to-end platform for treating unresectable liver tumours.

The Holmium Platform consists of three integrated products that allow you to select patients with confidence, deliver treatment with precision and plan and verify with accuracy.

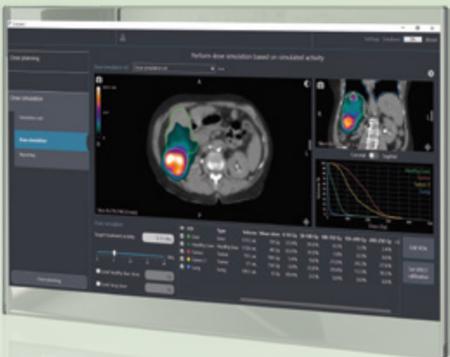
The Holmium Platform:
Delivering Individualized Treatment to the Right Patient



CONFIDENCE
in patient selection



PRECISION
in delivering SIRT as planned



ACCURACY
in treatment planning and verification

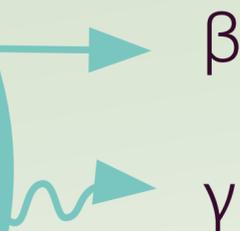
INNOVATION WITH HOLMIUM

QuiremSpheres® and QuiremScout® consist of Holmium-166 microspheres that offer unique imaging capabilities



PARAMAGNETIC

Holmium is highly paramagnetic and can be visualized with high-resolution using MRI



Holmium-166 decays under emission of beta radiation and a primary gamma photon (81 keV)

INNOVATION WITH HOLMIUM

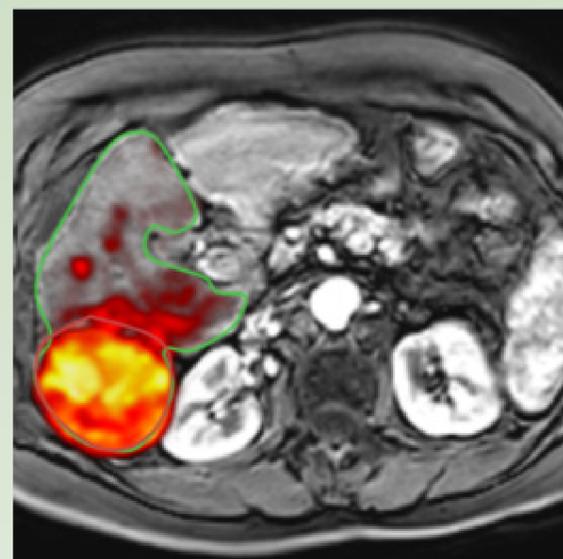
Holmium-166 microspheres allow for post-treatment visualization and quantification using MRI and SPECT, for further analysis in Q-Suite™

“QuiremSpheres® gives us the confidence we need to start individualizing treatments”

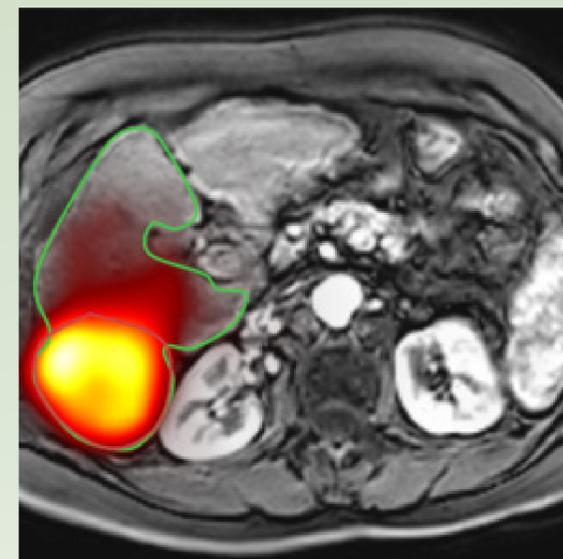
Prof. Dr. Ralf-Thorsten Hoffmann
Head of Interventional Radiology, University Hospital Dresden



MRI-based dose reconstruction



SPECT-based dose reconstruction



SIRT WITH THE HOLMIUM PLATFORM



STEP 1
Patient Selection



STEP 2
Treatment Planning



STEP 3
Treatment Delivery



STEP 4
Dose Verification



SELECT THE RIGHT PATIENTS, WITH CONFIDENCE

QuiremScout[®]: the first SIRT work-up product that uses the same technology as the therapeutic microspheres, to optimize patient selection and advance treatment planning



QuiremScout[®] contains the same microspheres as QuiremSpheres^{®1}

	^{99m} Tc-MAA	QuiremScout [®] ¹⁶⁶ Ho	QuiremSpheres [®] ¹⁶⁶ Ho
Particle morphology			
Material	MAA	PLLA	PLLA
Particle size (µm)	1-150	25-35	25-35
Number of particles (million)	0.2-1.2	3	15 - 30

QuiremScout[®] has been shown to be safe in a study of 82 patients^{2,3}

1. QuiremScout[®] 166Ho-Scout – Instruction for use. Available at: <https://www.quirem.com/ifu/>
 2. Braat et al. Eur Radiol 2018;28:920-28
 3. Prince et al. J Nucl Med 2015;56:817-23

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THE TREATMENT
FLOW



STEP 1
Patient Selection



STEP 2
Treatment Planning



STEP 3
Treatment Delivery



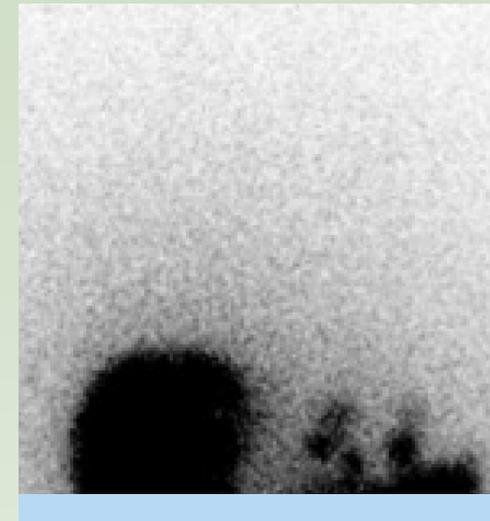
STEP 4
Dose Verification

SELECT THE RIGHT PATIENTS, WITH CONFIDENCE

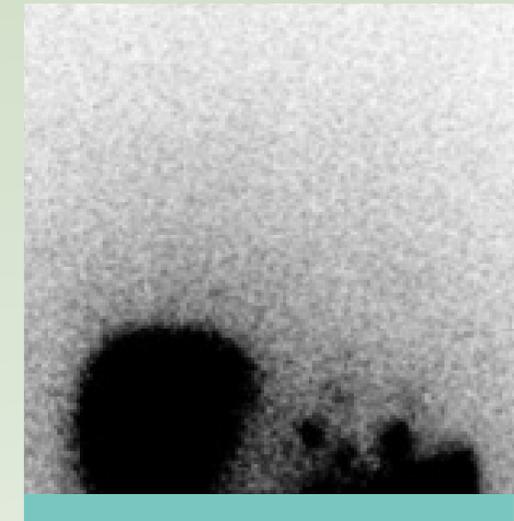
QuiemScout®: has been shown to be a better predictor for lung shunt and intrahepatic distribution than ^{99m}Tc-MAA^{4,5}



Predicted lung dose
 30 Gy based on
^{99m}Tc-MAA



Predicted lung dose
 0.02 Gy based on QuiemScout®



Lung dose
 0.01 Gy after QuiemSpheres®

4. Elschot et al. Eur J Nucl Med Mol Imaging 2014;41:1965-75

5. Dassen et al. Presented at CIRSE 2018. Abstract available at: <https://library.cirse.org/cirse2018/crs/the-predictive-value-of-the-intrahepatic-distribution-of-99mtc-macroaggregated-albumin-and-holmium-166-scout-dose-prior-to-holmium-166-radioembolization>

6. Grosche-Schlee et al. QuiemScout® case study. Available at: https://www.terumo-europe.com/en-emea/clinical-program/Clinical%20Data/E_Clinical_Case_Studies_QuiemScout_LR.PDF#search=SIRT%20case%20study

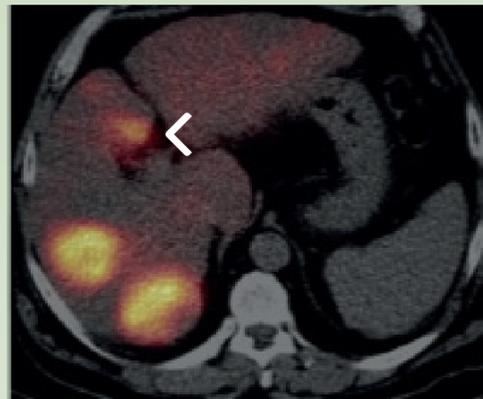
7. Smits et al. Eur J Nucl Med Mol Imaging 2020;47:798-806

8. Chiesa and Maccauro. Eur J Nucl Med Mol Imaging 2020;47:744-47

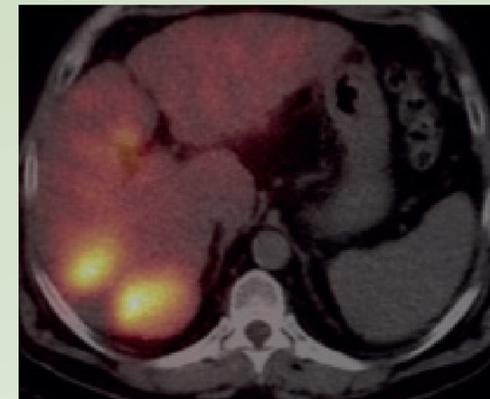
SELECT THE RIGHT PATIENTS, WITH CONFIDENCE

Case example

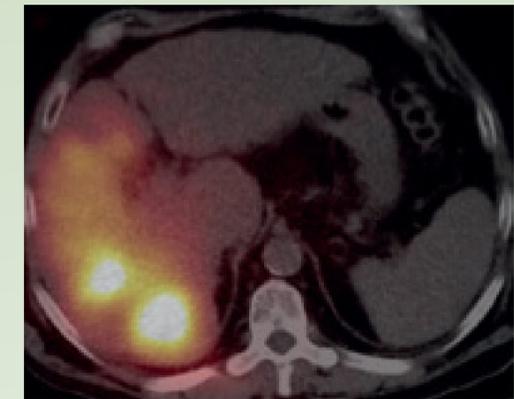
QuiremScout® has been shown to be more accurate at treatment planning than ^{99m}Tc-MAA, ensuring the right patients are identified for SIRT⁶⁻⁸



Extrahepatic accumulation of ^{99m}Tc-MAA in gall bladder
 = **Physician decision that SIRT was not possible**



No accumulation in gall bladder or elsewhere outside the liver with QuiremScout®
 = **Decision to proceed with SIRT was made due to little/no gallbladder uptake with QuiremScout®**



The post-treatment distribution of **QuiremSpheres®** was almost identical to the distribution of QuiremScout®

4. Elschof et al. Eur J Nucl Med Mol Imaging 2014;41:1965-75

5. Dassen et al. Presented at CIRSE 2018. Abstract available at: <https://library.cirse.org/cirse2018/crs/the-predictive-value-of-the-intrahepatic-distribution-of-99mtc-macroaggregated-albumin-and-holmium-166-scout-dose-prior-to-holmium-166-radioembolization>

6. Grosche-Schlee et al. QuiremScout® case study. Available at: https://www.terumo-europe.com/en-emea/clinical-program/Clinical%20Data/E_Clinical_Case_Studies_QuiremScout_LR.PDF#search=SIRT%20case%20study

7. Smits et al. Eur J Nucl Med Mol Imaging 2020;47:798-806

8. Chiesa and Maccauro. Eur J Nucl Med Mol Imaging 2020;47:744-47

CASE STUDY⁹

“ [This patient], originally deemed to be a non-surgical candidate, underwent a curative resection after radioembolization with QuiremSpheres® ”

Dr. Irene Bargellini, Head of Radiology, Cuneo Hospital

CT findings:

Female, 69 years old
Hx: obesity, arterial hypertension

Hospitalized for trauma:
Mild increases of GGT and AST

Undergoes CT examination

73 mm

- 1 **Biopsy:** iCC
- 2 **Resection:** GIST

Treatment decision for iCC:
work up for SIRT

9. Bargellini I et al. Presented at ECIO 2019. Available at: <https://library.cirse.org/ecio2019/events/2019-04-09-13-00-terumo-sirt-is-back-welcome-to-quiremscout>

CASE STUDY⁹

“ [This patient], originally deemed to be a non-surgical candidate, underwent a curative resection after radioembolization with QuiremSpheres® ”

Dr. Irene Bargellini, Head of Radiology, Cuneo Hospital

Timeline: March-July 2018, **July 2018**, December 2018, February 2019, March 2019

Work-up for SIRT, using ^{99m}Tc-MAA

Ineligible for SIRT because of gallbladder uptake

Treatment decision for iCC: systemic therapy

9. Bargellini I et al. Presented at ECIO 2019. Available at: <https://library.cirse.org/ecio2019/events/2019-04-09-13-00-terumo-sirt-is-back-welcome-to-quiremscout>

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THE TREATMENT FLOW

STEP 1 Patient Selection

STEP 2 Treatment Planning

STEP 3 Treatment Delivery

STEP 4 Dose Verification

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[This patient], originally deemed to be a non-surgical candidate, underwent a curative resection after radioembolization with QuiremSpheres®

Dr. Irene Bargellini, Head of Radiology, Cuneo Hospital

March-July 2018 July 2018 **December 2018** February 2019 March 2019

6 months' follow up

Total LV: 1475 cc
FLR (S2-S3): 587 cc (39%)

60 mm

Resection ruled out because:

- Obesity and presence of steatosis
- Chemotherapy for 6 months
- Elevated bilirubin and GGT
- Proximity of lesion to IVC

Resection ruled out

Treatment decision, QuiremScout® workup

9. Bargellini I et al. Presented at ECIO 2019. Available at: <https://library.cirse.org/ecio2019/events/2019-04-09-13-00-terumo-sirt-is-back-welcome-to-quiremscout>

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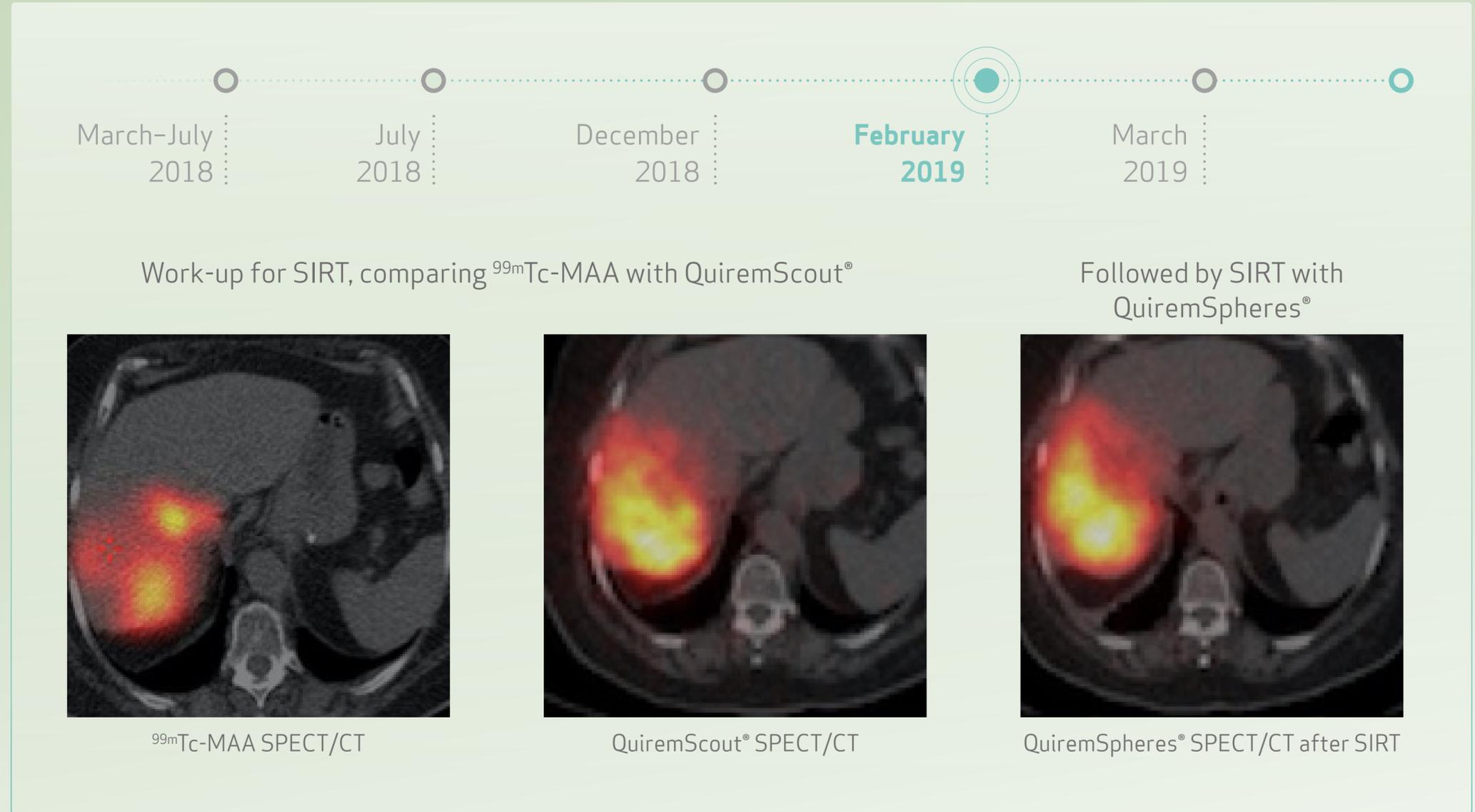
STEP 3
Treatment Delivery

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Dose Verification

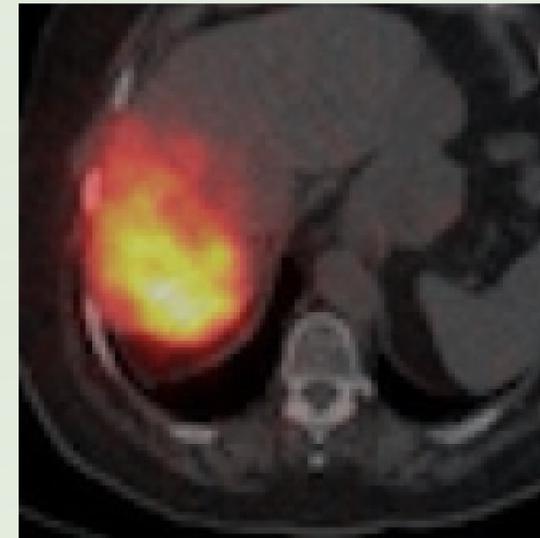
CASE STUDY⁹

[This patient], originally deemed to be a non-surgical candidate, underwent a curative resection after radioembolization with QuiremSpheres®

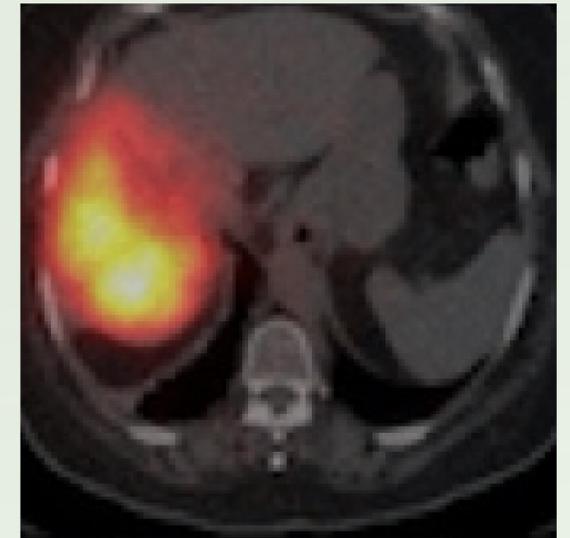
Dr. Irene Bargellini, Head of Radiology, Cuneo Hospital



^{99m}Tc-MAA SPECT/CT



QuiremScout® SPECT/CT



QuiremSpheres® SPECT/CT after SIRT

9. Bargellini I et al. Presented at ECIO 2019. Available at: <https://library.cirse.org/ecio2019/events/2019-04-09-13-00-terumo-sirt-is-back-welcome-to-quiremscout>

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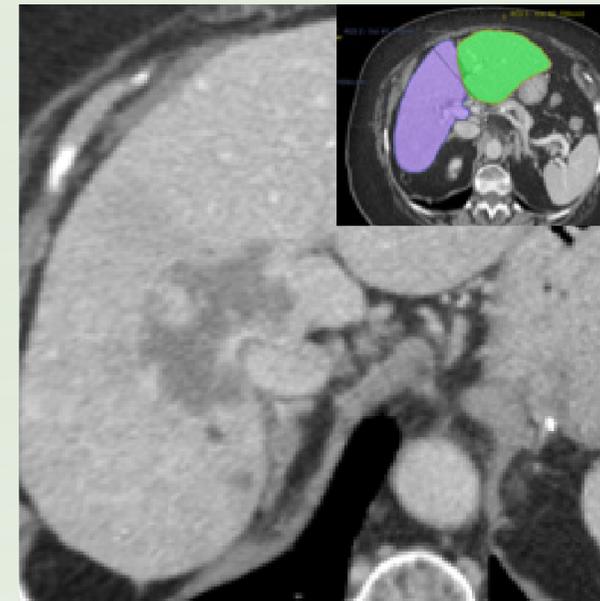
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“ [This patient], originally deemed to be a non-surgical candidate, underwent a curative resection after radioembolization with QuiremSpheres® ”

Dr. Irene Bargellini, Head of Radiology, Cuneo Hospital



45 days' follow up after QuiremSpheres® SIRT



55 mm

Total LV: 1556 cc

FLR (S2-S3): 700 cc (45%)

FLR (S2-S3-part of S4): 780 cc (50%)

Treatment decision for iCC: Resection

9. Bargellini I et al. Presented at ECIO 2019. Available at: <https://library.cirse.org/ecio2019/events/2019-04-09-13-00-terumo-sirt-is-back-welcome-to-quiremscout>

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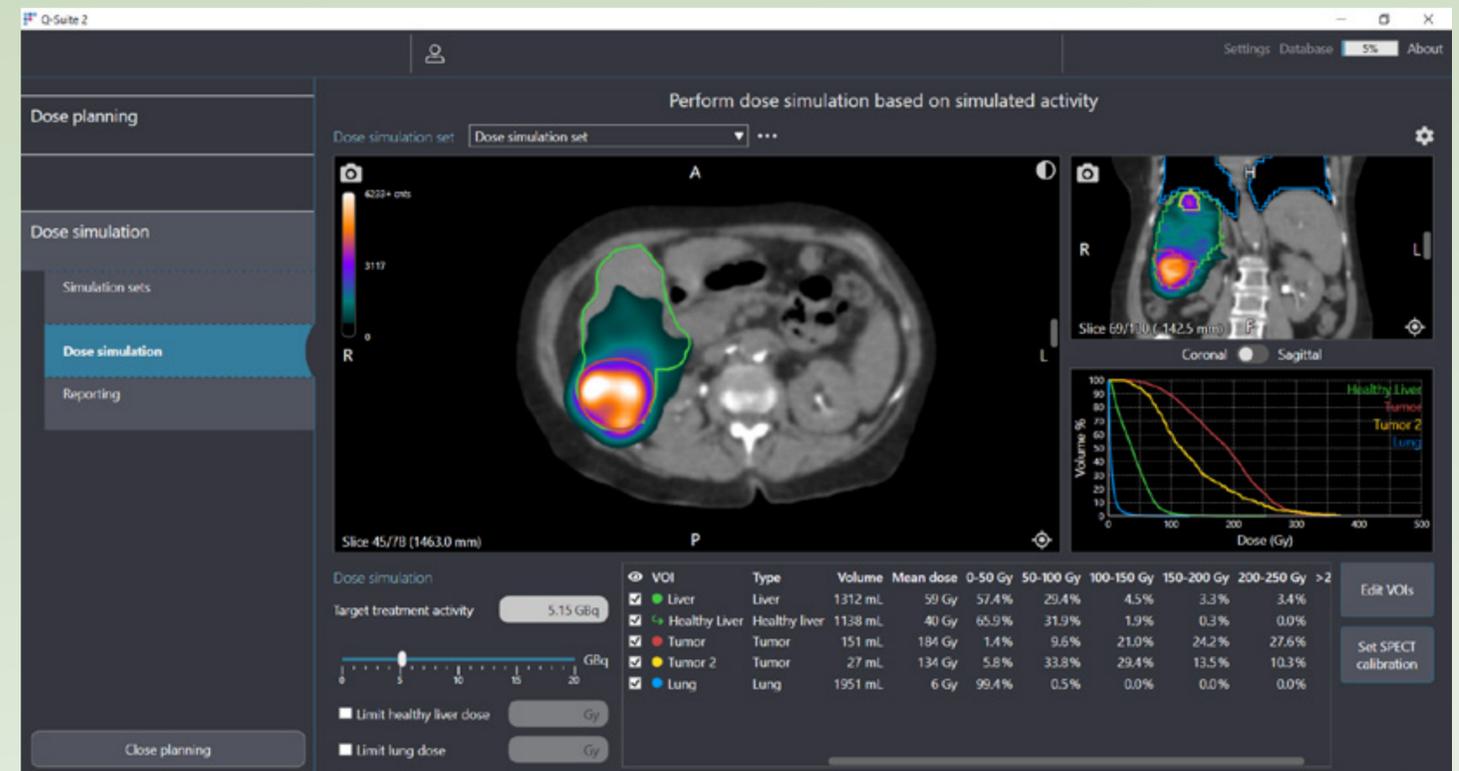
PLAN WITH ACCURACY

Q-Suite™:
Dedicated Holmium-166 software for individualized treatment planning

Treatment Activity Planning as recommended in QuiremSpheres® instructions for use

Lung Dose Prediction based on SPECT after QuiremScout® and/or Tc-99mMAA

Pre-Treatment Dose Simulation – Multi-compartment treatment planning based on QuiremScout® and/or Tc-99mMAA



DELIVER SIRT, AS PLANNED

QuiremSpheres®: The only therapeutic SIRT microsphere that is used as part of a fully integrated platform, to improve patient outcomes and advance the future of SIRT

The short half life of Holmium-166 in QuiremSpheres® ensures delivery of a high dose rate (90% of radiotherapy dose delivered within 4 days)

Clinical evidence demonstrates that QuiremSpheres® are efficacious¹⁰, well tolerated¹¹, and safe^{10,12} for the treatment of unresectable liver cancer

“With QuiremSpheres® we see the majority of our patients responding much quicker than what we are used to seeing with Yttrium-90®”

Dr. Irene Bargellini, Head of Radiology, Cuneo Hospital



10. Prince et al. J Nucl Med 2018;59:582-88
11. van Roekel et al. Clin Exp Metastasis 2020;37:95-105
12. Smits et al. Lancet Oncol 2012;13:1025-34

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THE TREATMENT FLOW



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Patient Selection



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STEP 3
Treatment Delivery



STEP 4
Dose Verification

DELIVER SIRT, AS PLANNED

Clinical case examples:



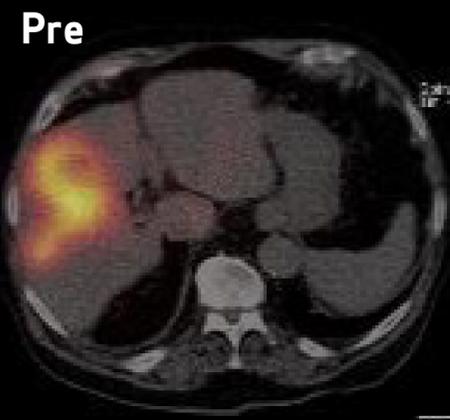
1. 84-year-old
HCC patient

Baseline Scan

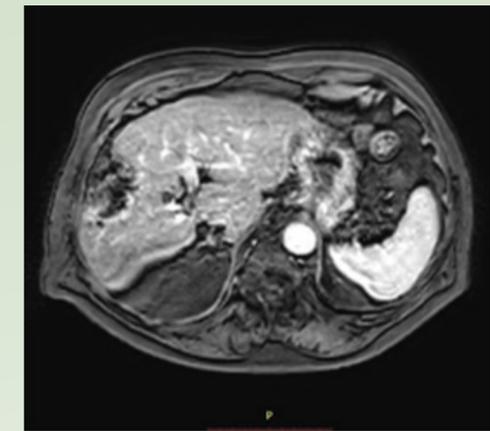


Large HCC tumours in segments IV, V, VI and VIII; plus two satellite lesions in segment VIII

QuiremScout[®] and treatment dose
Distribution Based on SPECT/CT



Follow-Up Scan



At 9 months
Complete response (including satellite lesions)

THE TREATMENT FLOW



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Treatment Planning



STEP 3
Treatment Delivery



STEP 4
Dose Verification

DELIVER SIRT, AS PLANNED

Clinical case examples:



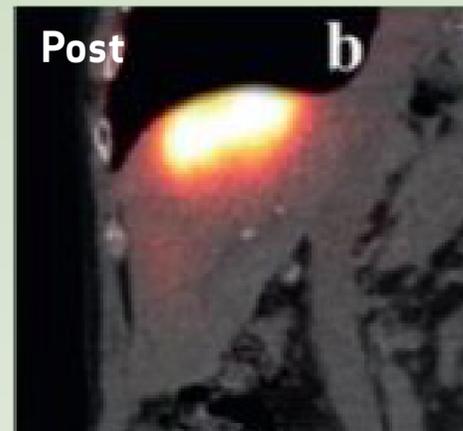
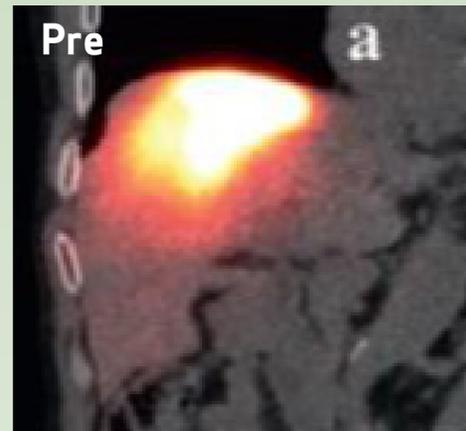
2. 80-year-old
mCRC patient

Baseline Scan



4 cm lesion traversing segments VII and VIII of the liver

QuiremScout[®] and treatment dose
Distribution Based on SPECT/CT



Follow-Up Scan



At 3 months

Complete response with sparing of the surrounding liver parenchyma

THE TREATMENT FLOW



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Treatment Planning



STEP 3
Treatment Delivery



STEP 4
Dose Verification

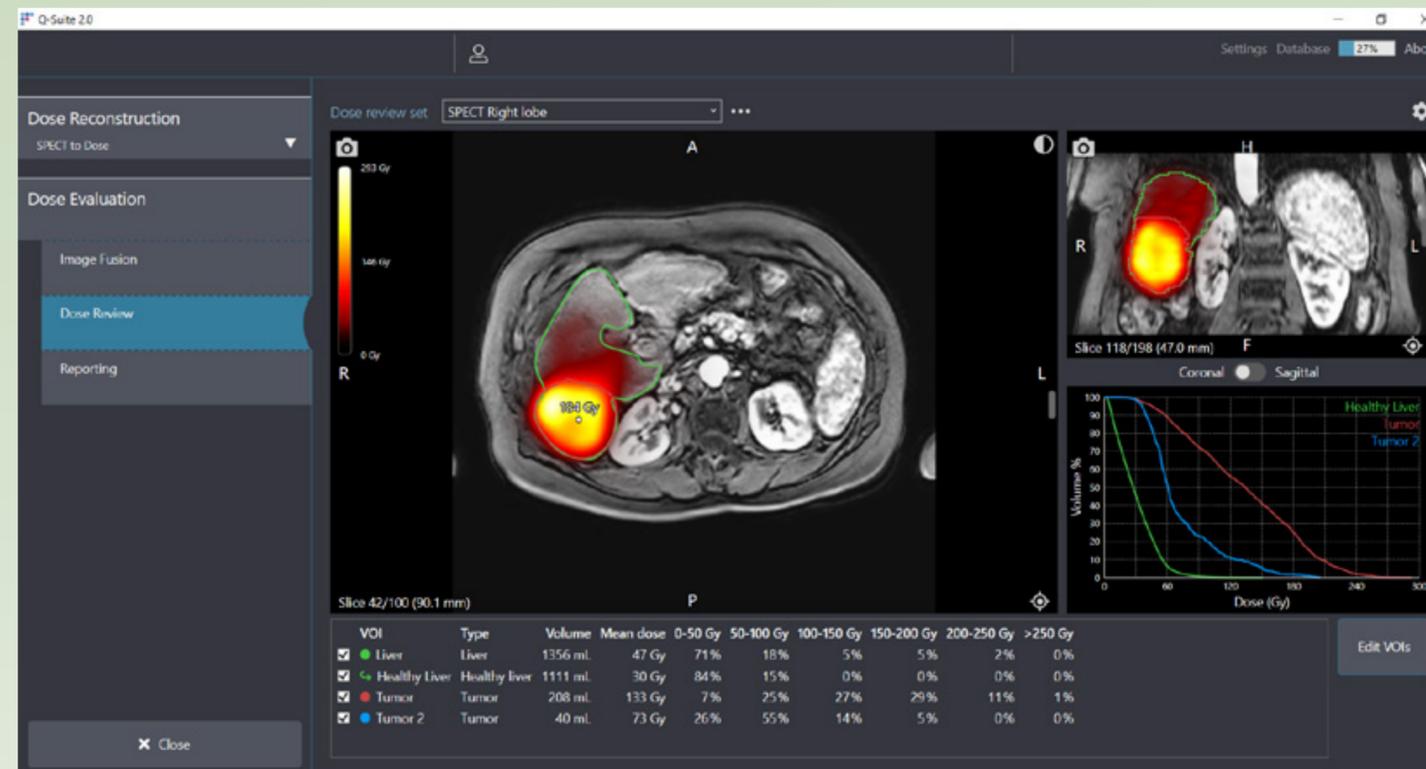
DOSE VERIFICATION

Q-Suite™:

accurate post-treatment dosimetry to verify the radiation dose delivered

Dose Reconstruction based on quantitative Holmium-166 MRI or SPECT

Evaluation of Dose absorbed in tumour and in healthy liver tissue



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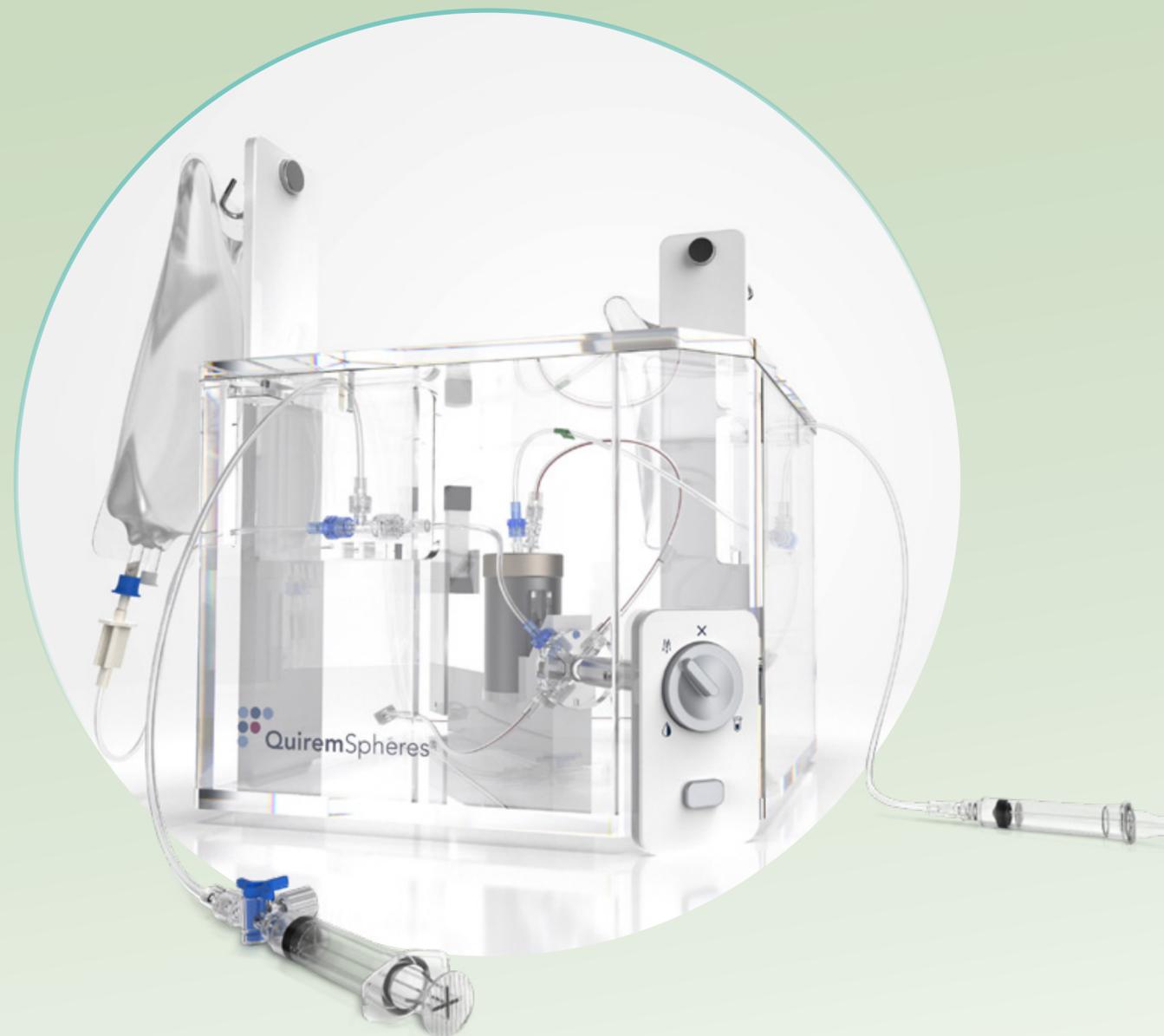
STEP 4
Dose Verification



DELIVER WITH EASE

QuiremSpheres® and QuiremScout® are administered using the same intuitive and efficient administration system

The system is easy to learn – it has been developed in collaboration with leading SIRT physicians and incorporates features that you may already be familiar with if you have performed SIRT.



UNPARALLELED SUPPORT

Full service set-up and support is provided, making it easy to start using The Holmium Platform in your centre



A comprehensive and tailored training program will be provided.



Full assistance to set up imaging systems for Holmium-166



Local QuiremSpecialist to support your daily clinical practice



ADDITIONAL TECHNICAL INFORMATION

Technical comparison of Holmium-166 and Yttrium-90

“We do not know which is ‘the best particle’ for radioembolization, but for sure we now know which is the best one nowadays for individual treatment planning [Holmium-166]”

Chiesa C and Maccauro M. 2020 EJNMMI

Isotope	Holmium-166 (QuiremSpheres® and QuiremScout®)	Yttrium-90	
		Resin (r)	Glass (g)
Beta radiation (MeV)	1.77 (48.7%) 1.85 (50.0%)	2.28	
Gamma radiation (keV)	81 (6.7%)	-	
Half life (h)	26.8	64.1	
Material	PLLA	Resin (r)	Glass (g)
Diameter (µm)	25-35	r: 20-60	g: 15-30
Density (g/cm ³)	1.4	r: 1.6	g: 3.3



AST, aspartate aminotransferase
 FLR, future liver remnant
 GGT, gamma-glutamyl transferase
 GIST, gastrointestinal stromal tumour

iCC, intrahepatic cholangiocarcinoma
 IVC, inferior vena cava
 LV, liver volume



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