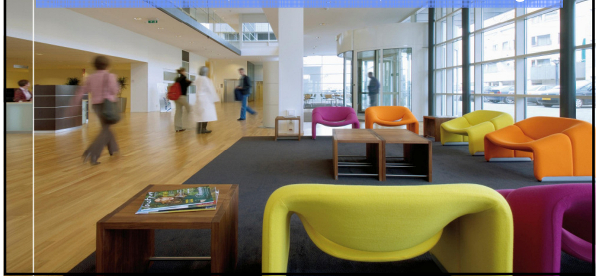
Towards real-time ultrasound image-guided abdominal radiotherapy

Skadi van der Meer, John Wong, Esther Bloemen, Davide Fontanarosa, Martin Lachaine, **Frank Verhaegen**



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History liver radiotherapy

- Prognosis after radiotherapy of liver cancer patients was poor
- Tumors needed a higher radiation dose for local control
- Impossible due to normal tissue constrains
- With current techniques, IMRT, SBRT, able to treat at higher dose levels without increasing the dose at organs at risks.
- Clinical trials demonstrated; highly effective to treat liver tumors with high dose levels

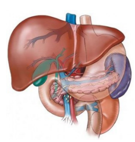

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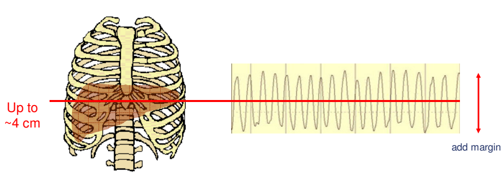
Image guidance of the liver

Accurate targeting liver lesions is a challenge:



→ assumption lesion moves within margin

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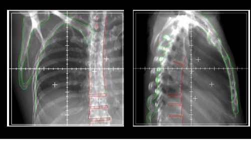
Image guidance for Liver SBRT

Accurate targeting liver lesions is a challenge with current techniques:

- Soft-tissue contrast is poor
- Lesions are not visible

Bone structures as alternative?

- Liver position
- Liver motion
- Liver deformation



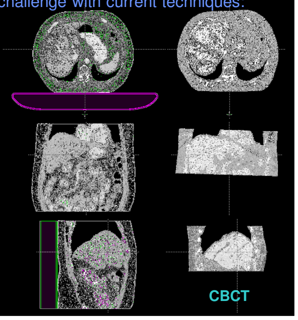


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Image guidance for Liver SBRT

Fiducials:

- Invasive
- Tumor spill
- Distance from lesion*
- Liver inflammation

KV cone-beam:

- Soft-tissue contrast not sufficient
- (Blurring due to breathing)

Criteria for the ideal IGRT solution

- Integrated with RT
- High precision
- Good resolution
- Soft-tissue contrast
- Non invasive
- Real-time imaging (live view)
- Also during treatment
- Not too expensive

US imaging:
Long term experience in diagnostic applications

*Seppenwoolde Y, Wunderink W, Wunderink-van Veen SR, *et al.* Treatment precision of image-guided liver SBRT using implanted fiducial markers depends on marker-tumour distance. *Phys Med Biol*;56:5445-5468.

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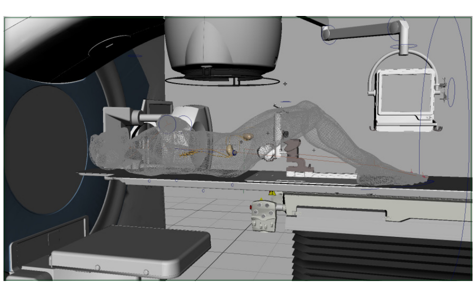
Clarity 4D prostate system (Elekta) : Novel transperineal ultrasound scan



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Towards abdominal, real-time, volumetric, soft-tissue image guidance with ultrasound

Combination of:

- 3DUS volumetric imaging
- 2DUS time series of the organ motion
- Robotic US probe placement
- US auto-contouring
- Contrast enhanced ultrasound (CEUS)

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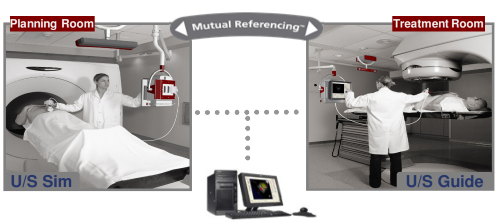
US image guidance

New modality: 3DUS for liver SBRT **Clarity 3DUS system** (Elekta)



Dosimetric consequences of misalignment and realignment in prostate 3DCRT using intramodality ultrasound image guidance. *Fraser DJ, Chen Y, Poon E, Cury FL, Falco T, Verhaegen F.* Med Phys 2010;37:2787-2795.

Dosimetric evolution of the breast electron boost target using 3D ultrasound imaging. *Fraser DJ, Wong P, Sultanem K, Verhaegen F.* Radiother Oncol. 2010 Aug;96(2):185-91

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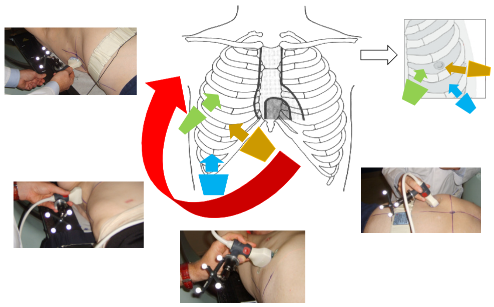
Overview of scan directions for Liver imaging



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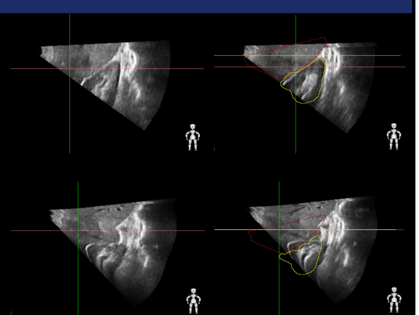
Feasibility study of IGRT with repeated 3D US imaging for liver lesions

breath hold

free breathing



→ image segmentation difficult

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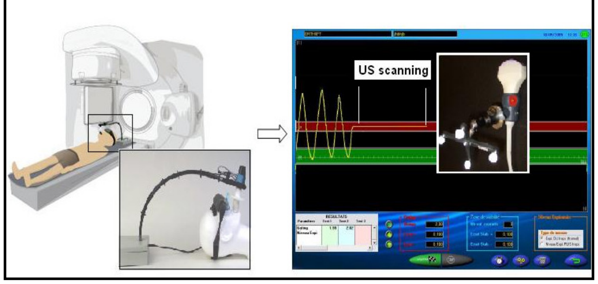
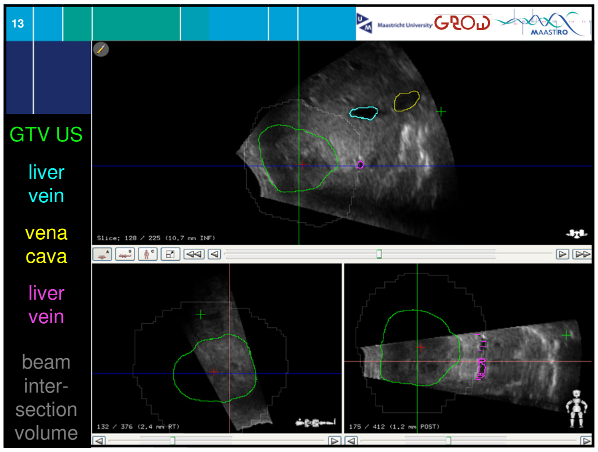
Breath hold control

To obtain US scans in breath hold, we used the SDX spirometer system (DynR, France)

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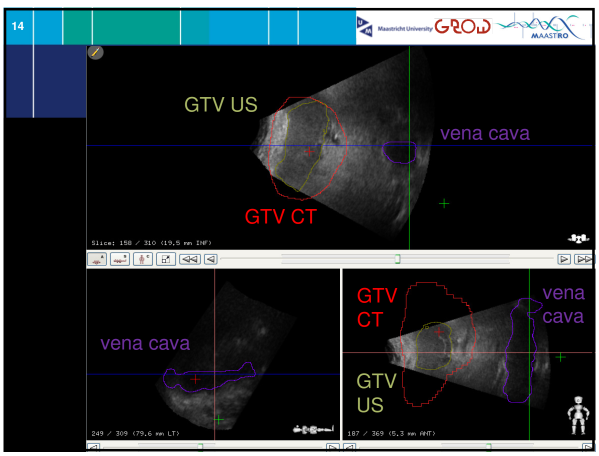
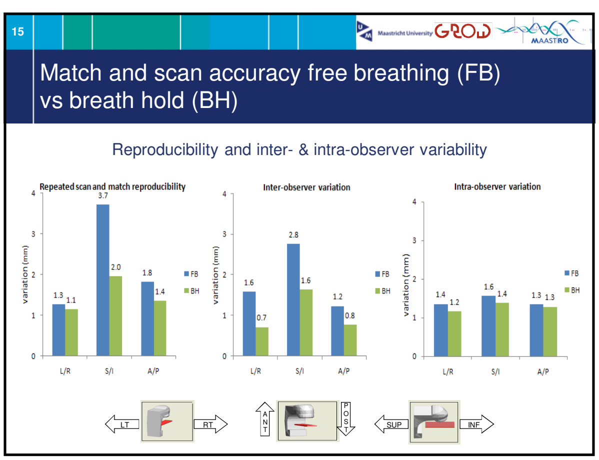
GTV US
liver vein
vena cava
liver vein
beam inter-section volume


14
GTV US
vena cava
GTV CT
vena cava
GTV CT
vena cava
GTV US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Match and scan accuracy free breathing (FB) vs breath hold (BH)
Reproducibility and inter- & intra-observer variability
Repeated scan and match reproducibility
Inter-observer variation
Intra-observer variation
variation (mm)
FB
BH
L/R
S/I
A/P
1.3
1.1
3.7
2.0
1.8
1.4
1.6
0.7
2.8
1.6
1.2
0.8
1.4
1.2
1.6
1.4
1.3
1.3
LT
RT
ANT
POST
SUP
INF

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3DUS volumetric imaging: Conclusion

- US scanning of liver lesions:
  - free breathing → causes artifacts, reducing image quality;
  - in a predefined breath hold phase → accurate
    (reference and daily scans are acquired with the liver in the same fixed position);
- The combined uncertainty (1SD) of US scanning and matching (inter and intra observer) :
  - in free breathing 4mm
  - in breath hold 2mm
- With 3D US imaging, accurate online interfraction image guidance of liver lesions and/or surrogates is feasible. → Recommended during breath hold.
- Nevertheless, integration of liver motion monitoring during treatment is still lacking

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Towards abdominal, real-time, volumetric, soft-tissue image guidance with ultrasound

Combination of:
- 3DUS volumetric imaging
- **2DUS time series of the organ motion**
- Robotic US probe placement
- US auto-contouring
- Contrast enhanced ultrasound (CEUS)

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2DUS time series with spatial information

Steady probe position and orientation

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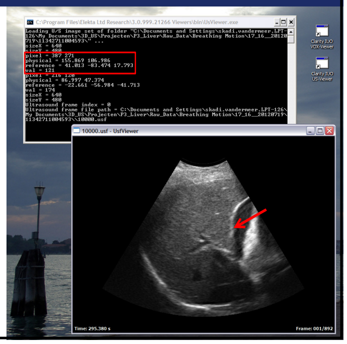
2DUS time series with spatial information

Dedicated software
- RAW data
- Spatial information



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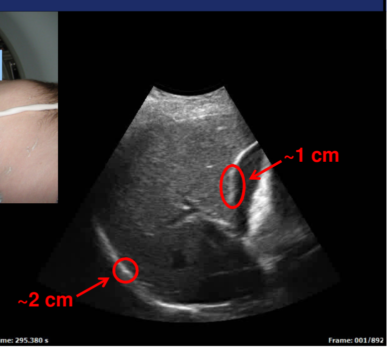
2DUS time series with spatial information



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Robot System Requirements

Research by the Johns Hopkins University School of Medicine, Baltimore

- Develop a robot system to:
  - Record placement of US probe by expert clinician during CT simulation
  - Assist general clinician to place US probe, considering recorded position, force, and image
  - Hold ultrasound probe (or dummy) in place during CT acquisition and radiation treatment

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Technical Approach

Research by the Johns Hopkins University School of Medicine, Baltimore

- Cooperative control with soft motion constraints (virtual fixtures):
  - Cooperative control: move robot by applying forces at the end-effector
  - Motion constraints: restrict motion to guide user to desired target
  - Soft motion constraints: allow motion away from desired target, but with larger effort

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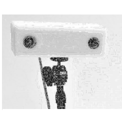
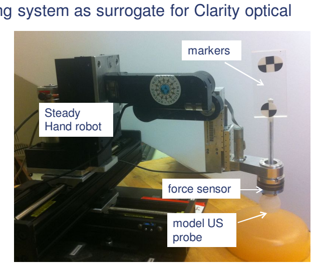
Prototype System

Research by the Johns Hopkins University School of Medicine, Baltimore

- Adapted existing JHU Steady Hand robot, initially designed for retinal microsurgery
- Use Claron Micron tracking system as surrogate for Clarity optical tracking system



Claron Micron Tracker



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Experimental Procedure

Research by the Johns Hopkins University School of Medicine, Baltimore

1. Use cooperative control to guide probe to target
2. Record information (position, force)
3. Starting from an arbitrary position, use cooperative control with soft virtual fixture to guide user back to target position
4. Measure position difference using optical tracking system and robot (possible because robot base not moved during experiment)
   – Optical tracking system is less accurate than robot

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Experimental Results

Research by the Johns Hopkins University School of Medicine, Baltimore

- Performed three trials:
  - 3 different targets
  - 3 different users
- In each trial:
  - user defines target
  - returns to target 3 times
- User Impressions:
  - Robotic assistance made it quick and easy to accurately reproduce initial placement

		Robot diff., mm	Tracker diff., mm
Trial 1	1	0.09	0.74
	2	0.05	0.38
	3	0.09	0.20
	Mean	0.08	0.44
Trial 2	1	0.13	0.75
	2	0.17	0.94
	3	0.15	0.57
	Mean	0.15	0.75
Trial 3	1	0.20	0.40
	2	0.11	0.36
	3	0.20	0.80
	Mean	0.17	0.52

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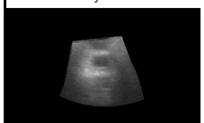
Automated Multimodal 3D Contouring for *Prostate* 3D Ultrasound

Research by TAlab Tecnologie Avanzate Srl, Udine, Italy

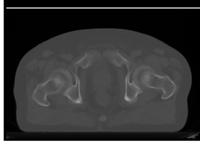
Problems with single modality contouring algorithm:

Low stability due to the lack of a complete set of features to detect the prostate boundary in CT and US images.



US:

- upper boundary → well enhanced
- lower boundary → sometimes a bit more confused
- Lateral boundaries → more confused



CT:

- sharp edges and high contrast between tissues with very different densities
- But not enough contrast in the soft-tissue range (like between prostate and its surrounding tissues)

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Multimodal 3D proposed algorithm

Research by TAlab Tecnologie Avanzate Srl, Udine, Italy

Full and direct use of all **3D information** available from a scan.

Easily extensible to a **multimodal approach**:

- retrieve information from different imaging modalities
- use them **simultaneously** in the segmentation process

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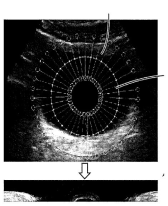
Algorithm

Research by TAlab Tecnologie Avanzate Srl, Udine, Italy



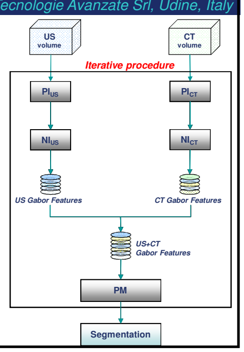
Projection of 3D data around current boundary into Projected Image (PI)
Extension to 3D of paradigm from [1]

Global and local normalization (Normalized Image)
Application of paradigm from [1]

Multiscale features extraction (Gabor)
as in [2]

Multimodal features concatenation

Generation of Probability Mask (PM) by unsupervised classifier (trained)



[1] "Methods and systems for segmentation using Boundary reparameterization", Koptenko et al. United State Patent Application Publication
[2] "Segmentation of Prostate Boundaries From US Images using statistical shap model", Shen et al. IEEE Transactions on Medical Imaging, Vol. 22, No. 4, April 2003

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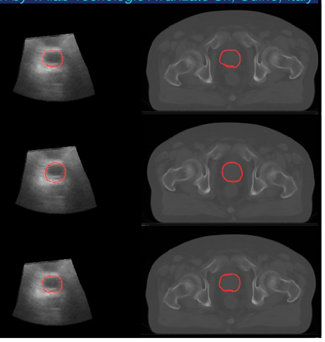
Example

Research by TAlab Tecnologie Avanzate Srl, Udine, Italy

Segmentation on US volume

Segmentation on CT volume

Segmentation on US+CT volume



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- **Contrast enhanced ultrasound (CEUS)**

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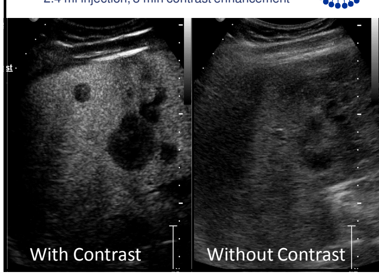
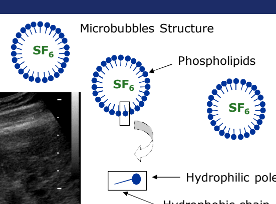
Contrast enhanced ultrasound imaging

Diffused liver metastases

2.4 ml injection, 8 min contrast enhancement





M.Schneider, M.Arditi, M.B.Barrau, J.Brochot, A.Broillet, R.Ventrone, and F.Yan. BR1 : A new ultrasonographic contrast agent based on sulfur hexafluoride-filled microbubbles. Investigative Radiology 1995 ; 30 (8) : 451-457.

M.Schneider. Characteristics of SonoVue®. Echocardiography 1999 ; 16 (7) Part 2 : 743-746.

Phase 3 SonoVue Multi-institutional trial for trans-abdominal imaging of liver lesions

(U. Hamper, JHU Principal Investigator)

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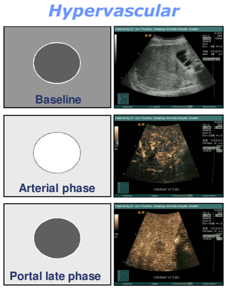
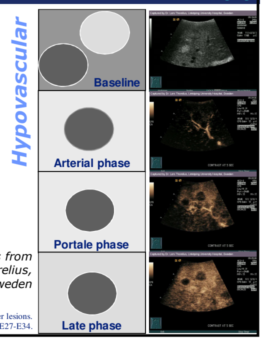
Metastasis

Bracco Imaging





Images from Dr Lars Thorelius, Linkoping, Sweden

Réf : E.Leen. The Role of contrast-enhanced ultrasound in the characterisation of focal liver lesions. Eur. Radiol 2001 ; 11 (suppl.3) : E27-E34.

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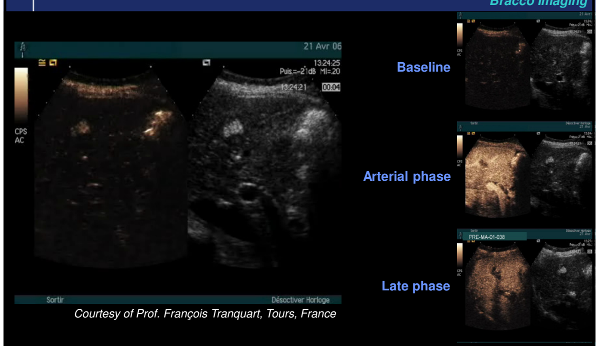
Liver Metastasis

Bracco Imaging



Courtesy of Prof. François Tranquart, Tours, France

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Combination of:
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- Contrast enhanced ultrasound (CEUS)

And beyond….

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And beyond………

Elastography (Young's modulus estimation)
[*European Urology,54:1354-62,2008*]

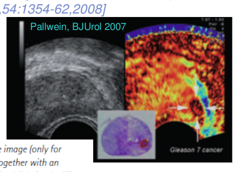
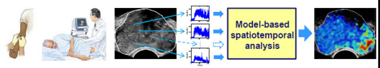


FIG. 3. Unsuspicious B-mode image (only for topographical orientation) together with an elastogram, showing a clearly visible focal stiffer area on the left side (mid-gland) fulfilling all the criteria for a suspicious lesion and presenting a cancer area. The corresponding histopathological slice confirms a Gleason 7 prostate cancer. The changes in elasticity in the inner gland and at the contralateral side do not fulfil all criteria for a suspicious lesion.

Tissue characterization

Histoscanning
(frequency spectrum classification)
[*BJU International,101:293-98,2008*]



Contrast Ultrasound Dispersion Imaging (CUDI)
Mischi et al, *IEEE IUS, 2009 & IEEE TUFFC, in press.*
Kuenen et al, *IEEE IUS, 2010 & IEEE TMI, 2011.*
Smeenge et al, *World J Urol, 2011.*

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Acknowledgements

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Silvia Pesente
Francesco Pascoli

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Denis Ermacora

Bracco Imaging:
Bart Beyloos