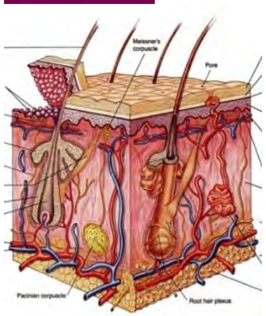
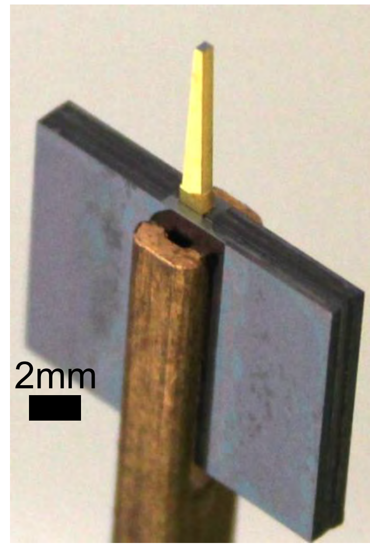
Our approach...

microwaves



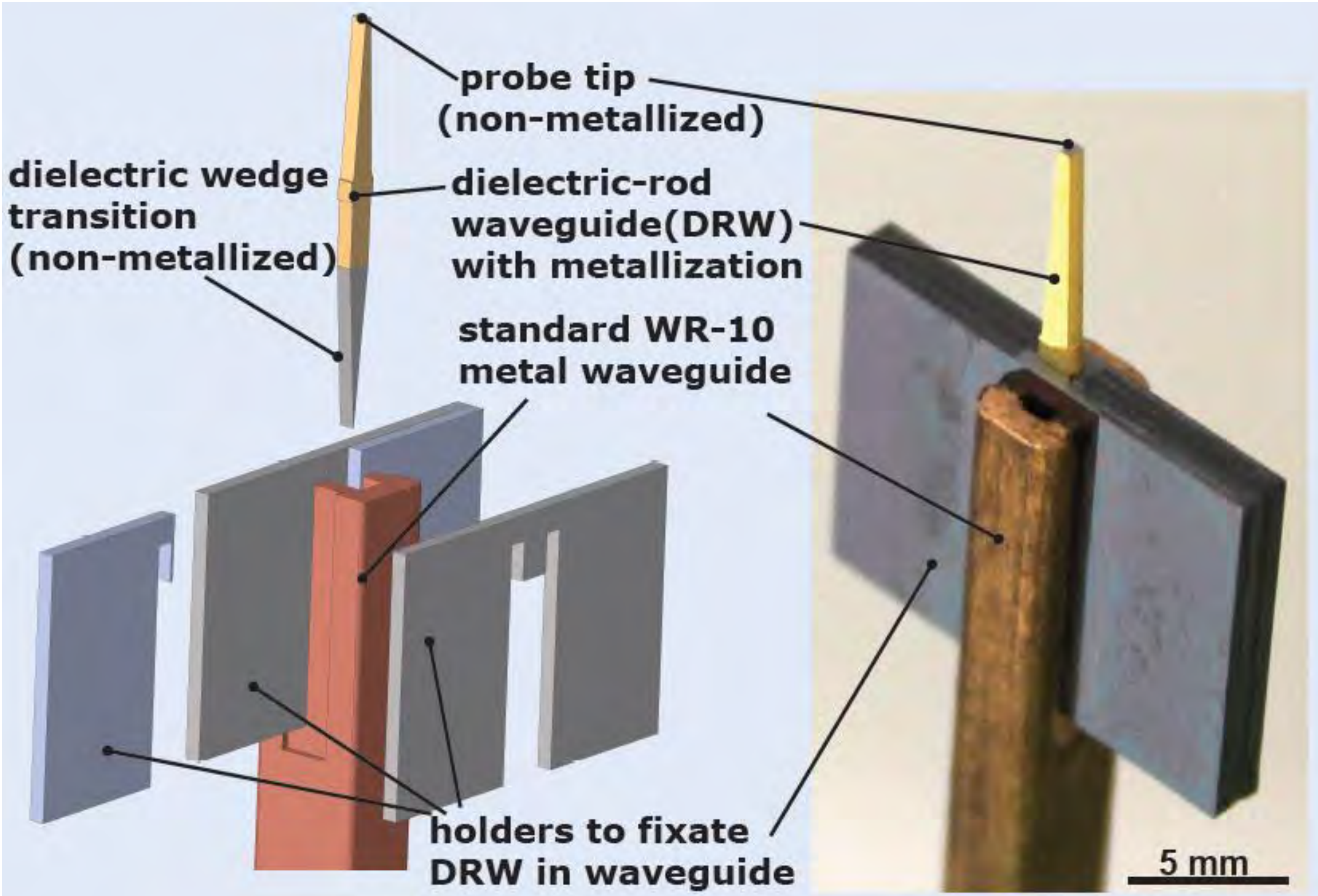
medical
diagnosis

micro-machining



Micromachined, high-resolution, microwave diagnostic tool for skin cancer

KTH's micromachined mm-wave skin-cancer probe

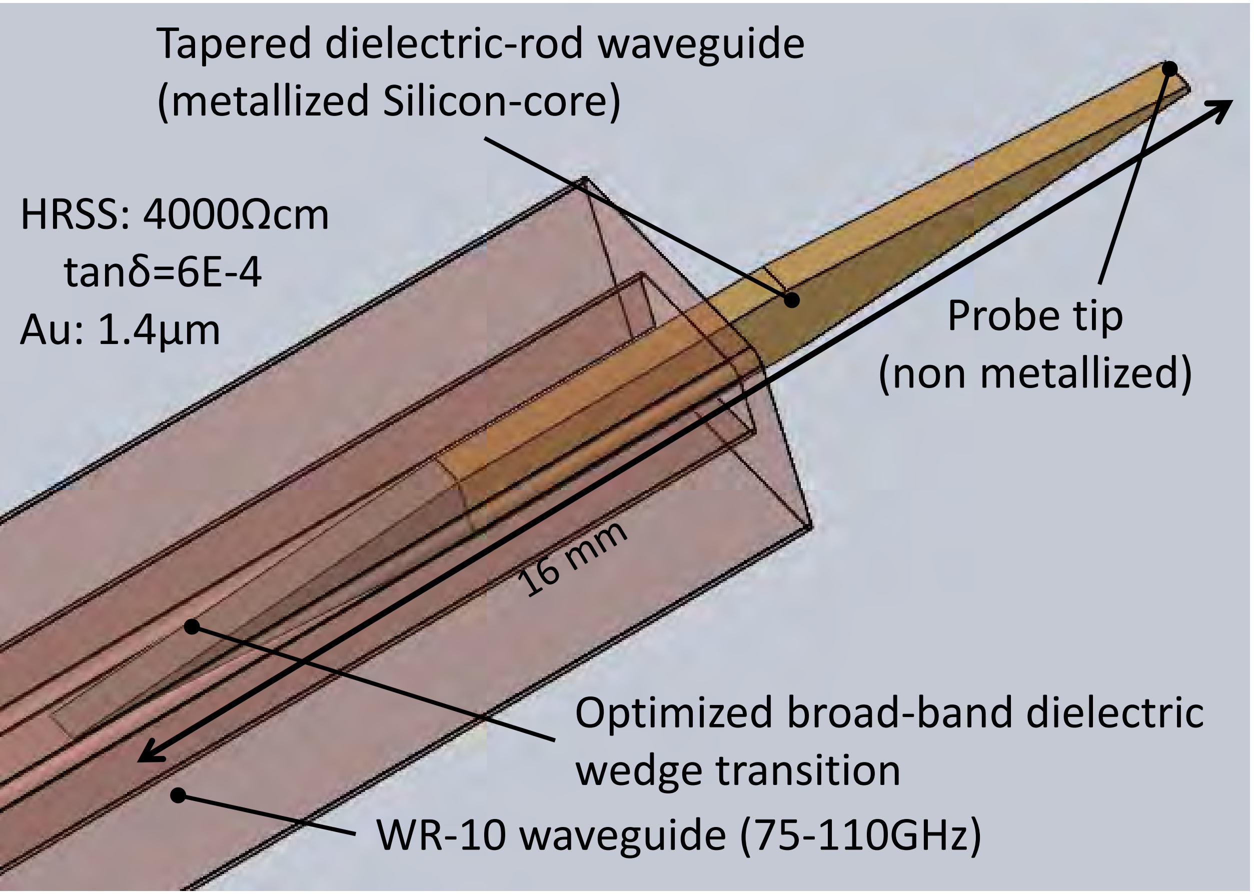


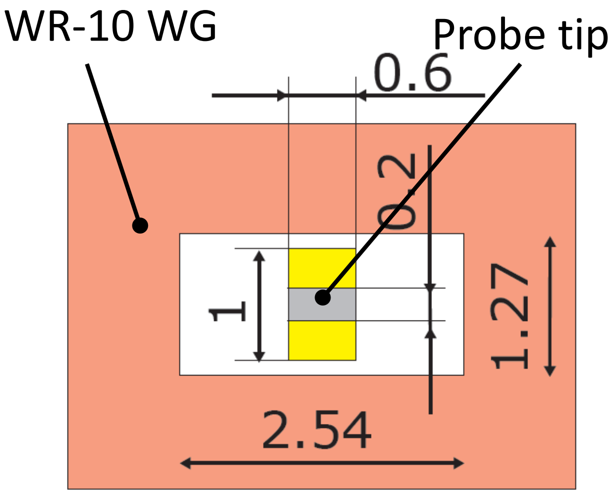
Töpfer, Dudorov, Oberhammer, *IEEE IMS 2012*.

Probe size and design

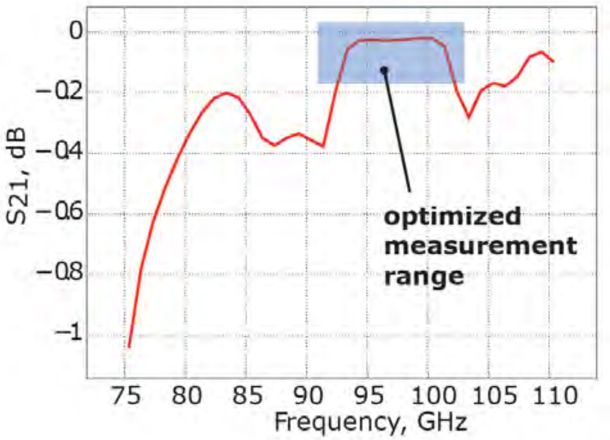
Subwavelength probe tip size:
0.2λ in skin tissue at 100GHz

HRSS: 4000Ωcm
tanδ=6E-4
Au: 1.4µm



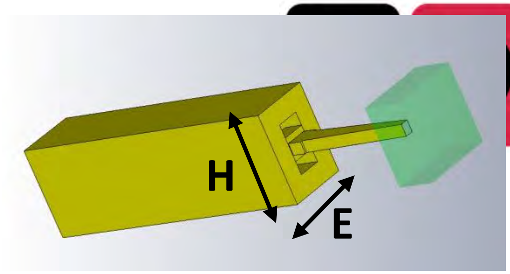


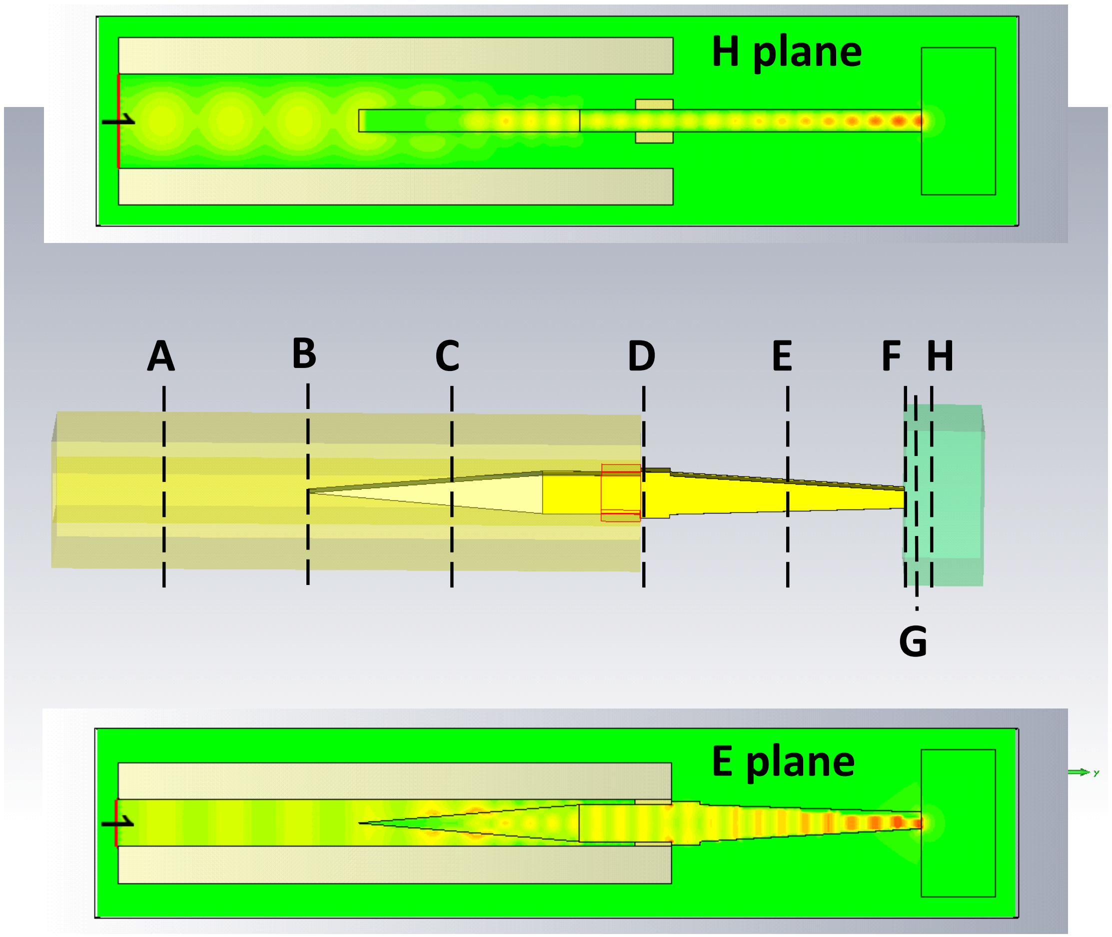
(dim. in mm)

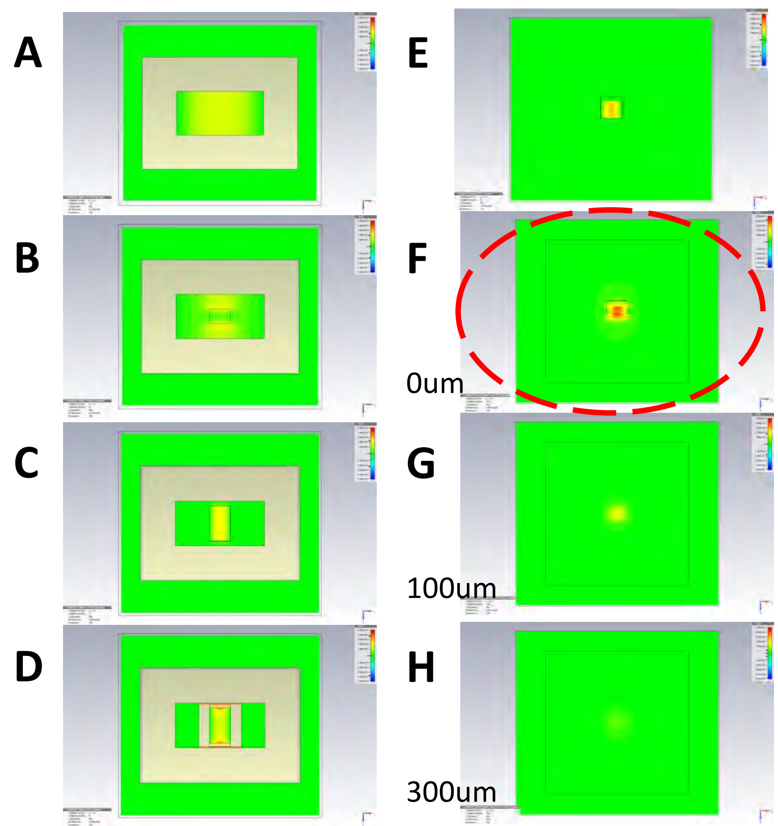


Töpfer et al, *IEEE IMS 2012*.

Design & simulations



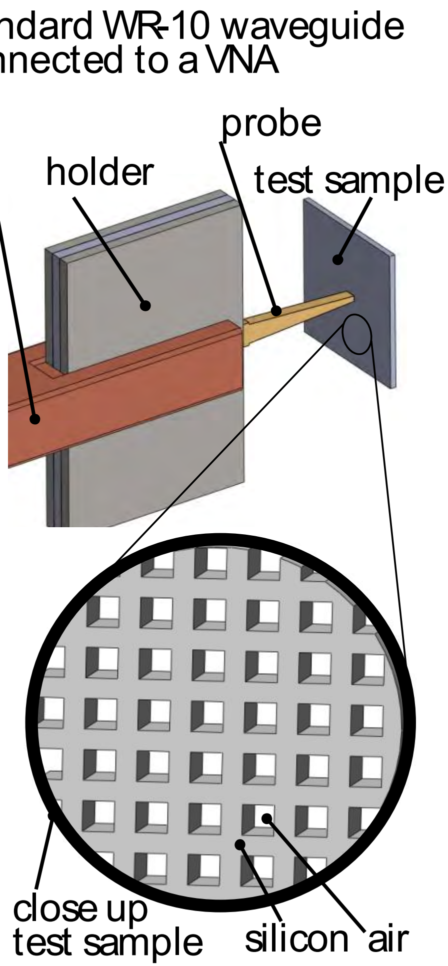


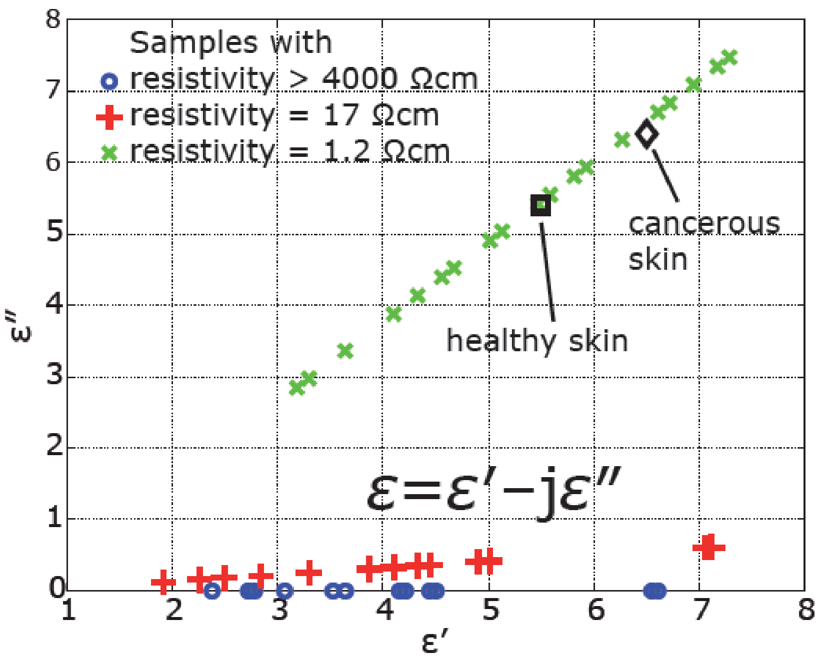


@100 GHz

CST Microwave Studio, FDTD

Calibration with silicon of ‘tailor-made’ permittivity



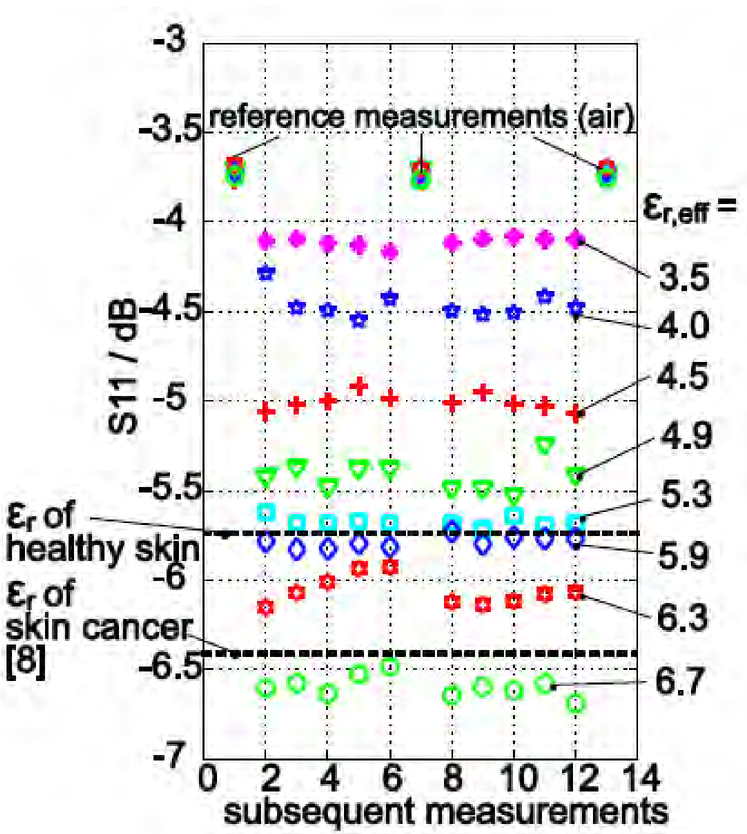


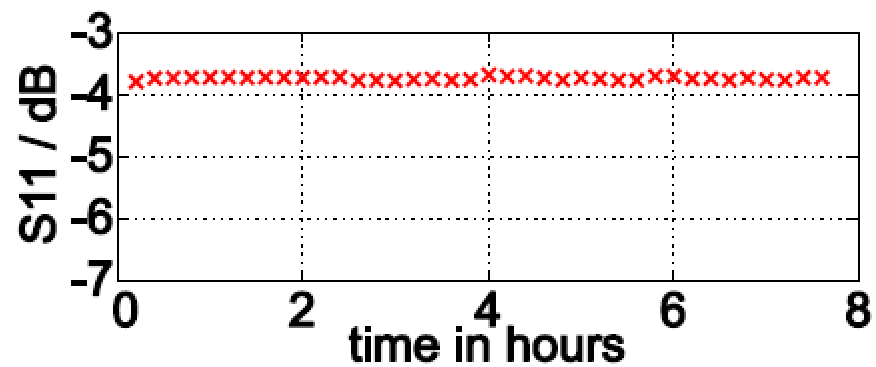
Sub-wavelength perforated silicon:

- permittivity by design from 1.5 to 10
- losses by using doped substrate
- micromachined (DRIEtched)

Töpfer, Dudorov, Oberhammer, *IEEE MEMS 2013*.

Technical probe characterization

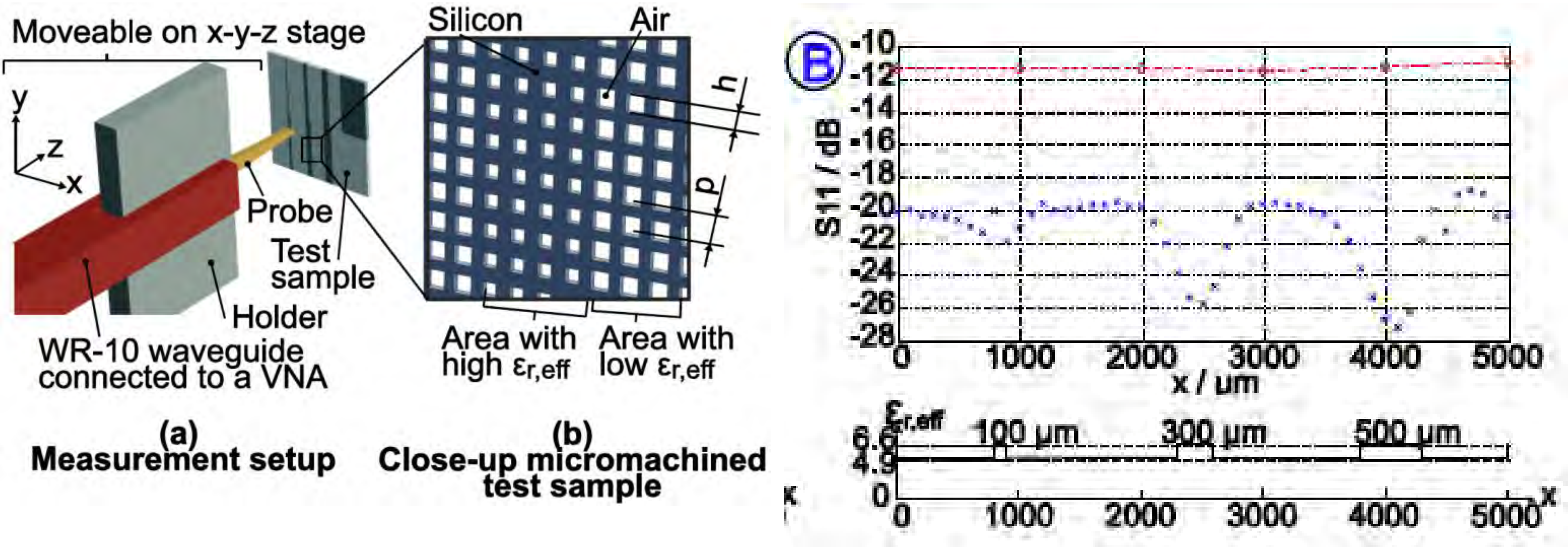




- high responsivity
- high reproducibility (<1.5%)
- high stability (<0.6%/6h)

Töpfer, Dudorov, Oberhammer, *IEEE IMS 2012*.

Probe resolution



- lateral resolution ~100um
- tested on tailor-made samples mimicking permittivity modulation corresponding to healthy and cancer tissue

Töpfer, Dudorov, Oberhammer, *IEEE MEMS 2013*.

Part 5. In-vivo studies

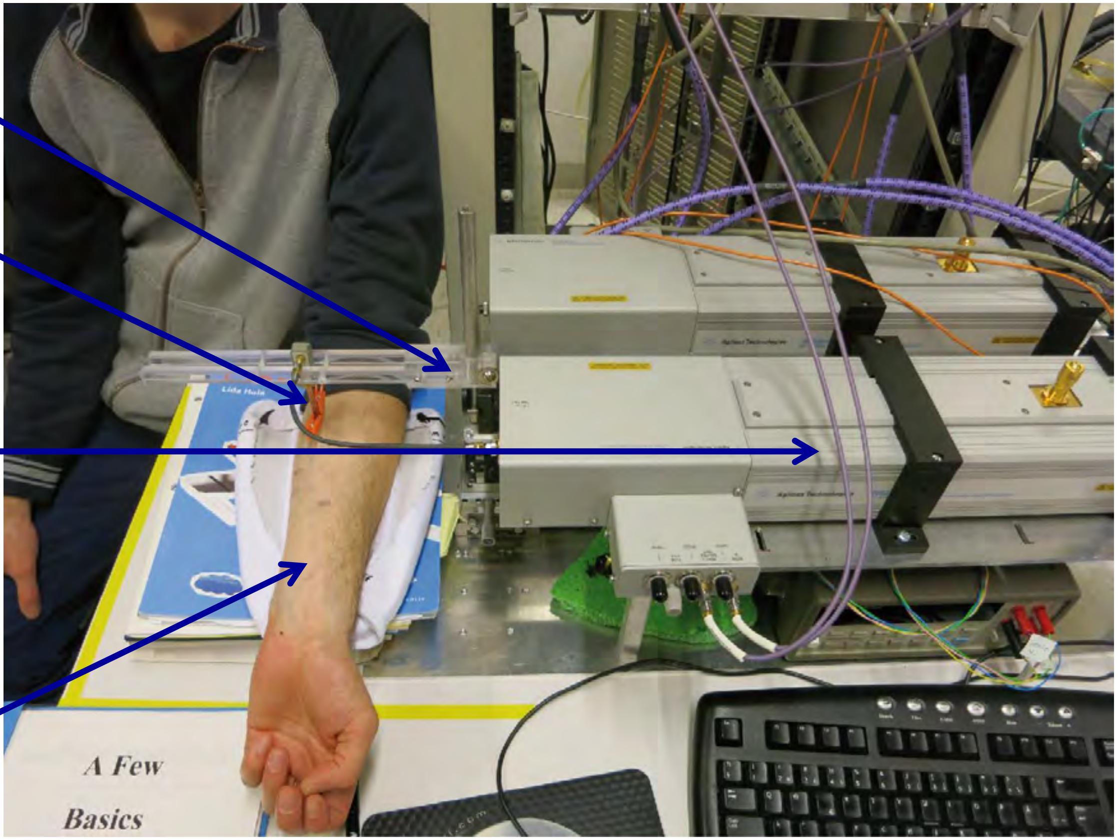
Measurement setup for on-skin measurements

X-y-z stage to move probe onto and over skin

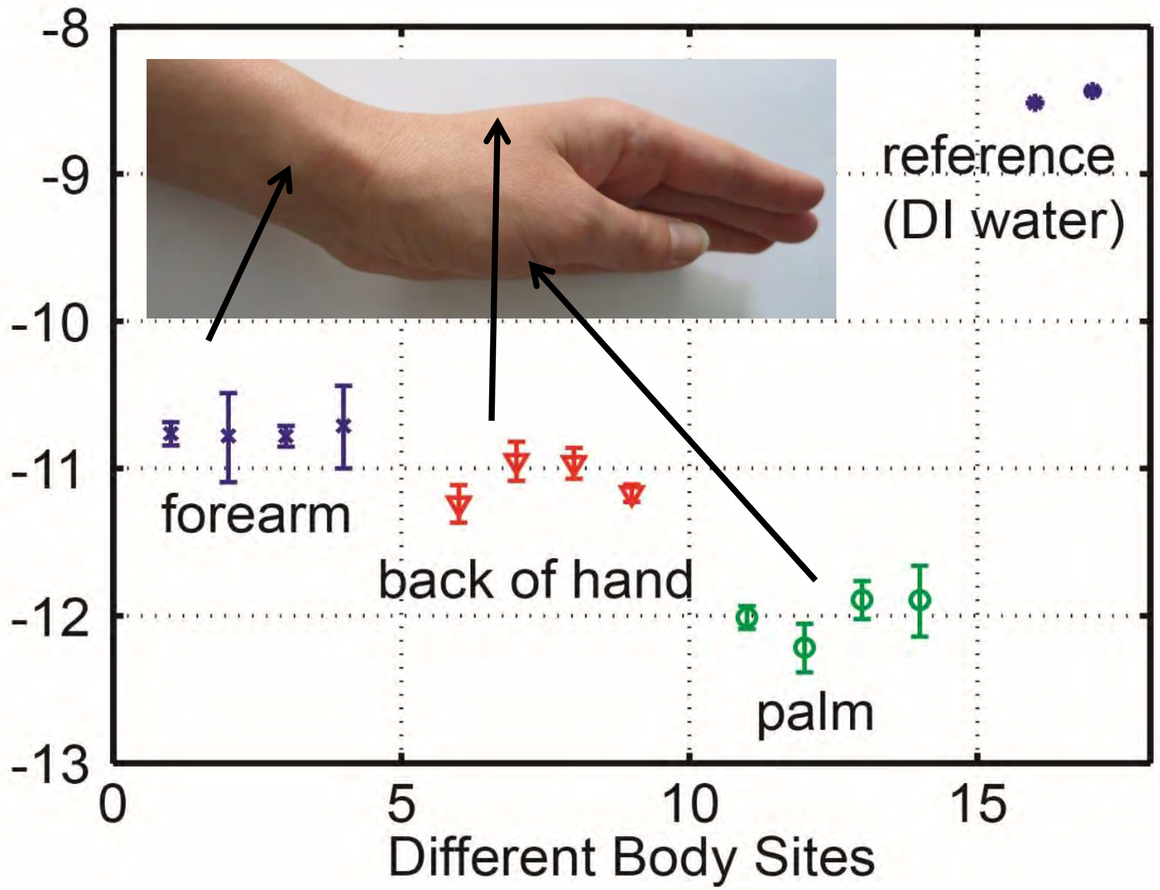
Micromachined millimeter-wave probe, connected to VNA through standard waveguide

E8163A Agilent vector network analyzer (VNA) with millimeter-wave extender heads, up to 110 GHz

Arm of test subject (here: my supervisor)



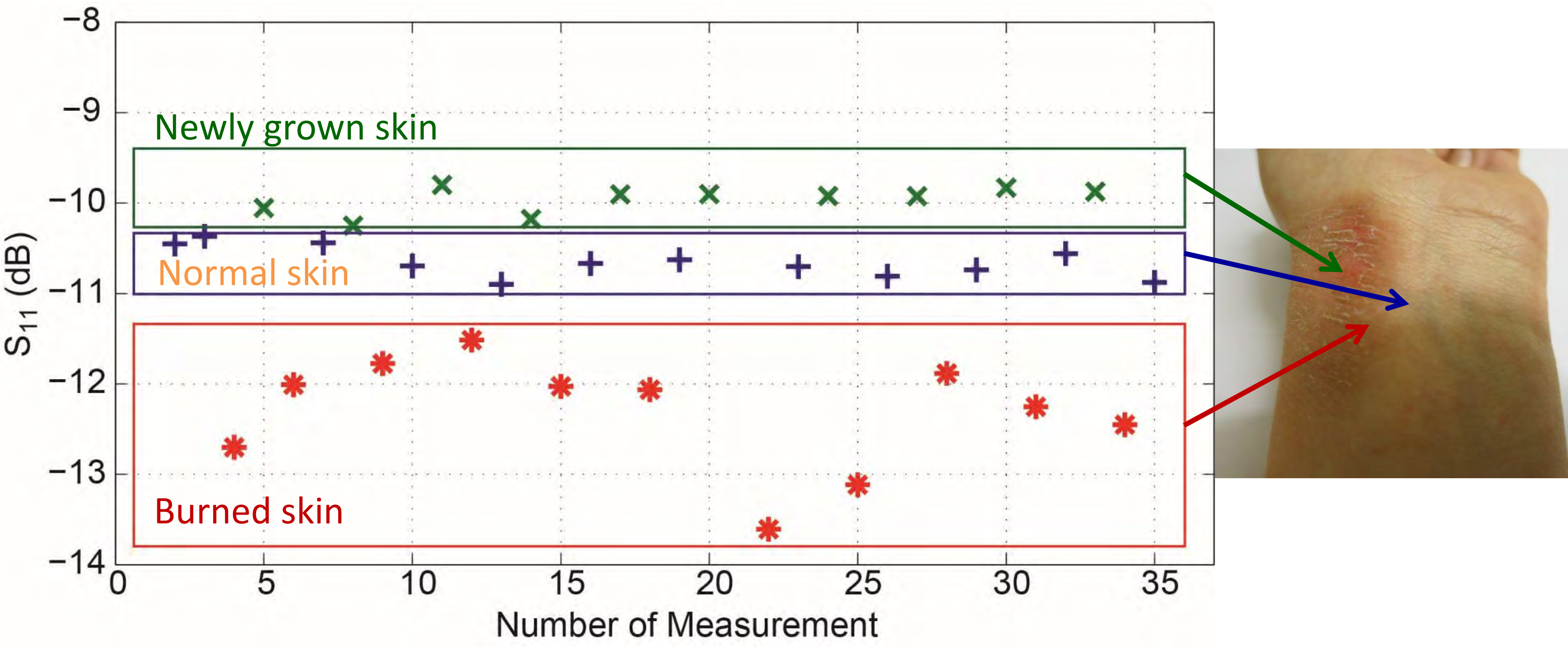
Measurements on different body sites



- Different S_{11} measured on different body sites → for skin cancer diagnostics reference measurement on surrounding tissue required

Töpfer, Dudorov, Oberhammer, *IEEE IMS 2014*.

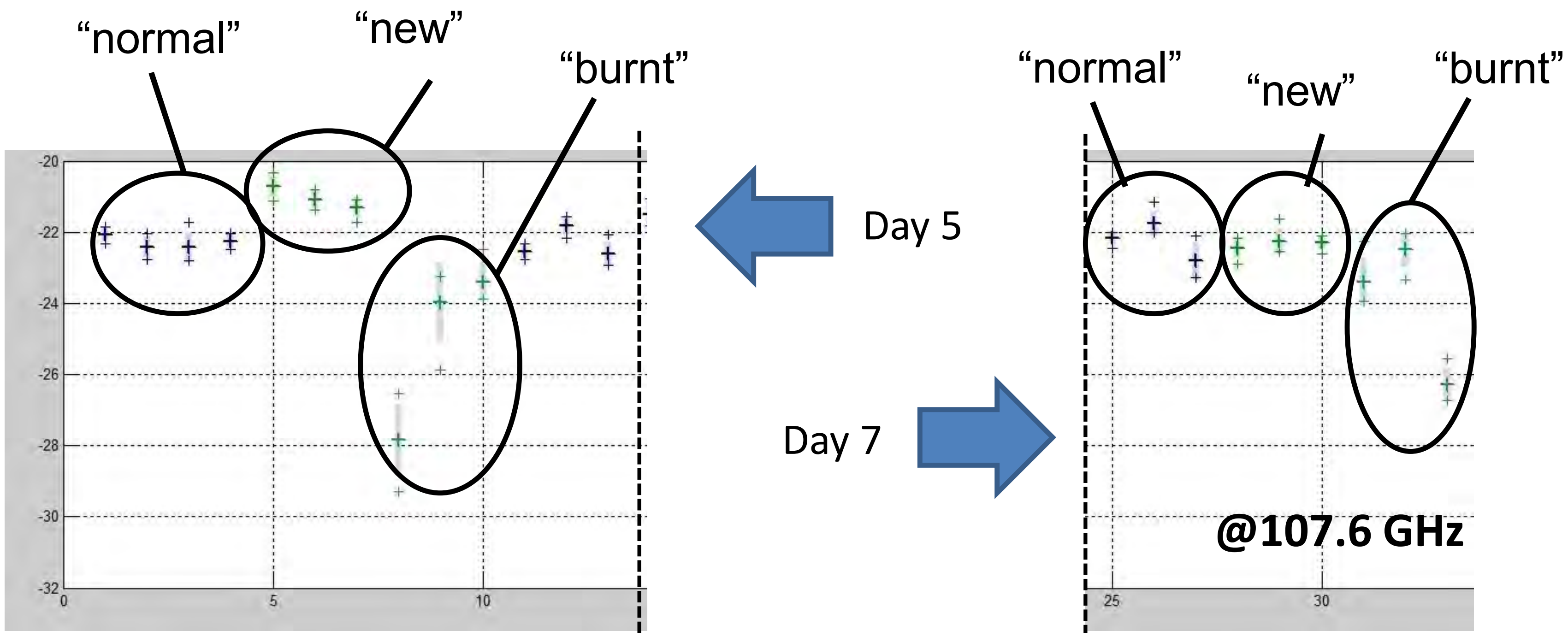
Skin burn measurements



- Clear differences in S_{11} measurements with our mm-wave probe between burned, newly grown and normal skin.

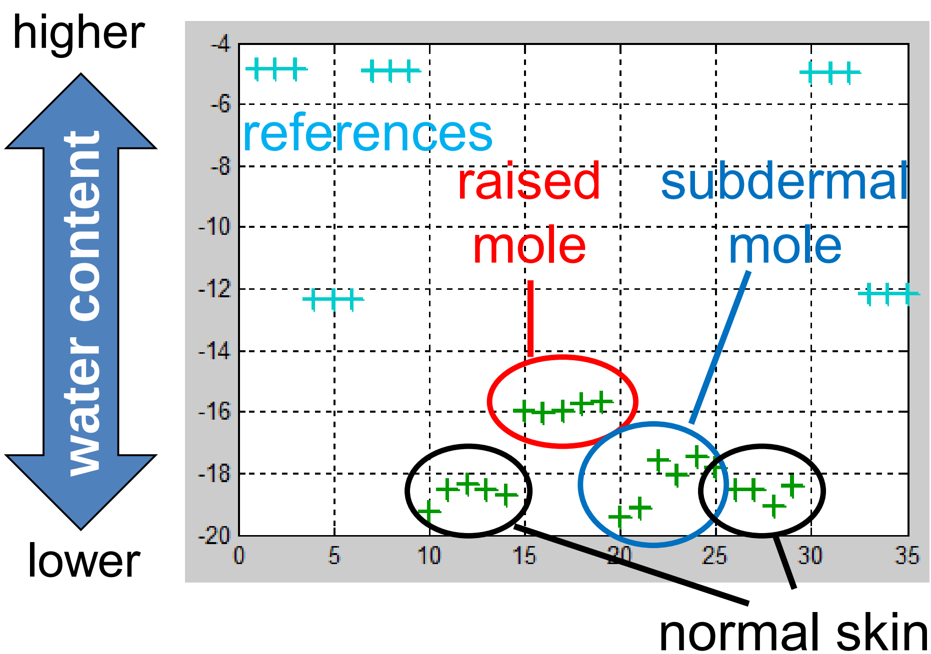
Töpfer, Dudorov, Oberhammer, *IEEE IMS 2014*.

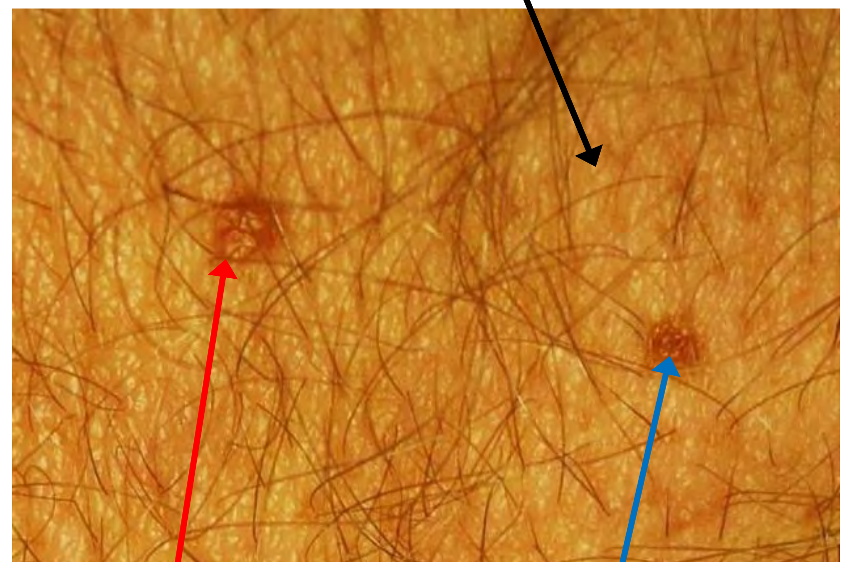
Monitoring of skin healing process



- day 5: normal/new/burnt still distinguishable
- day 7: normal/new indistinguishable; burnt approaching normal

Discrimination benign skin neoplasms from subdermal nevi





Profile scan over intradermal nevus

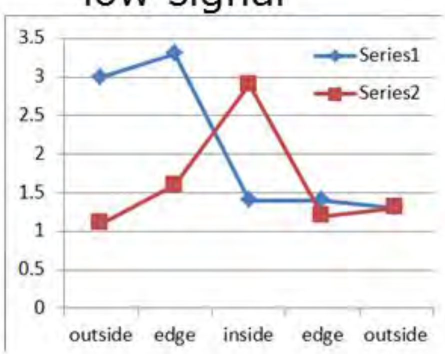
ROYAL INSTITUTE OF TECHNOLOGY

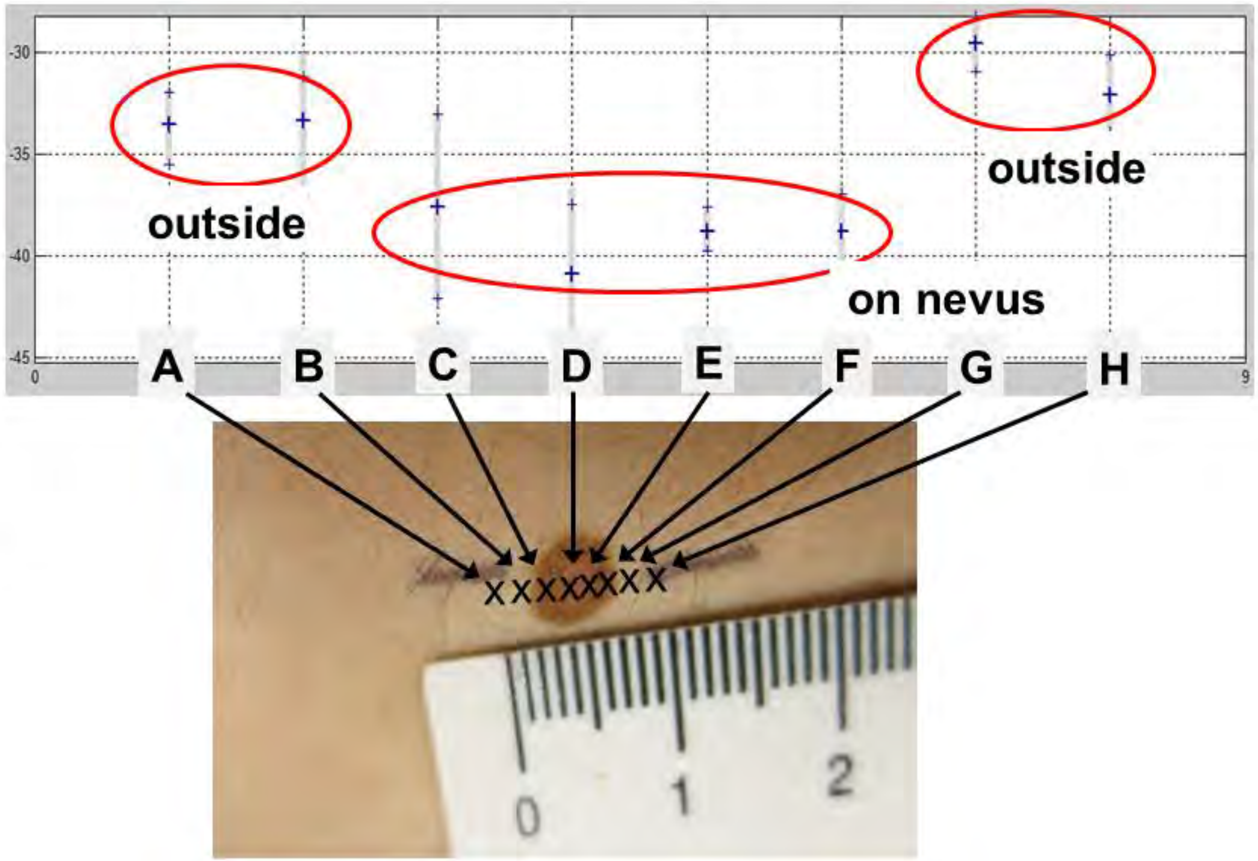
KTH microwave measurements:

- clear correlation with nevus

TEWL reference measurements

- not stable/reproducible
  low signal





Töpfer, Dudorov, Oberhammer, *IEEE IMS 2014*.

Standardized dermatological tests

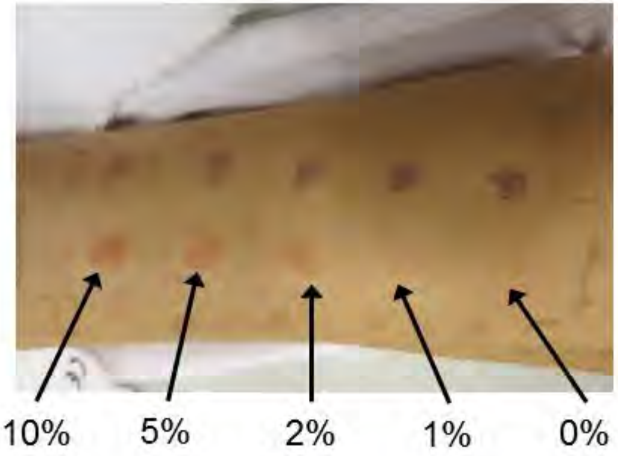
- artificially stimulated skin irritation with chemicals, similar to allergy tests
- patches with different concentration levels (0%, 1%, 2%, 5%, 10%) applied for 24 hours
- monitored every day
- references:
  - examination by dermatologist
  - trans-epidermal water-loss instrument

Töpfer, *IEEE IMS 2014*.

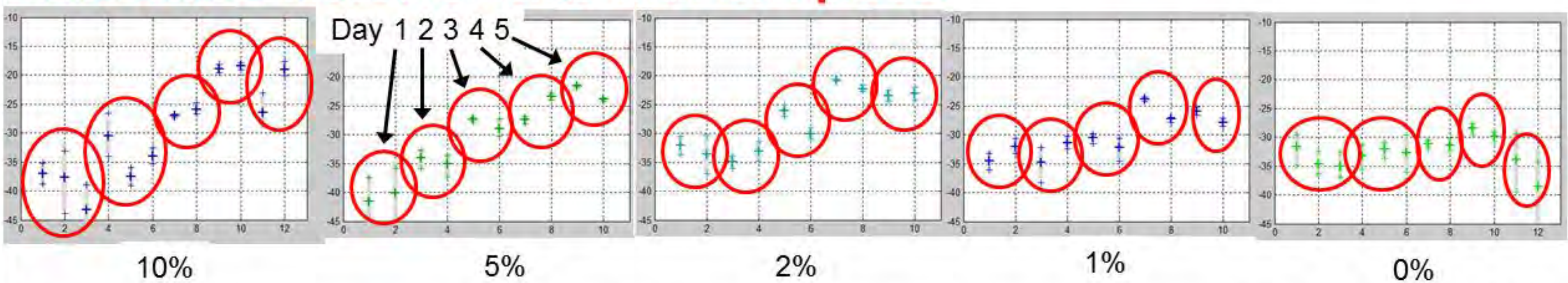
Monitoring of irritant skin reactions

ROYAL INSTITUTE OF TECHNOLOGY

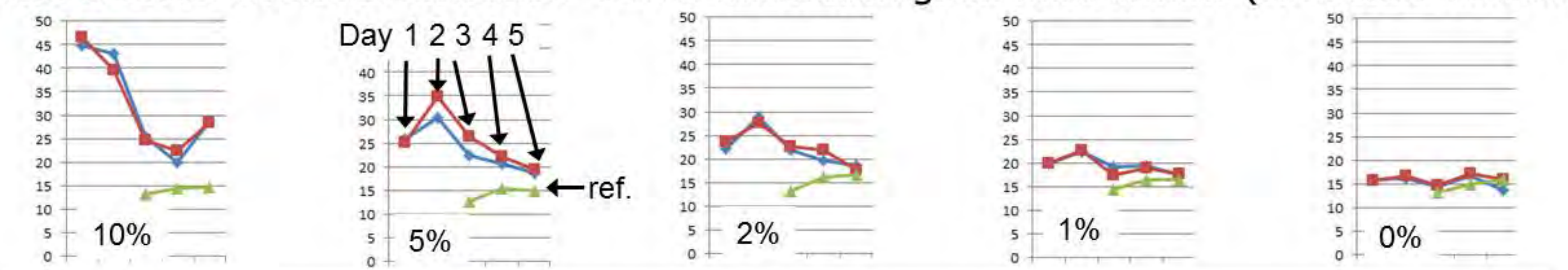
skin irritation with sodium-lauryl-sulphate
(24 hours, 10%, 5%, 2%, 1%, 0%)



- **Microwave measurements with KTH probe:**

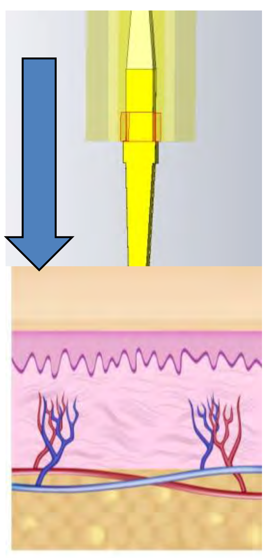


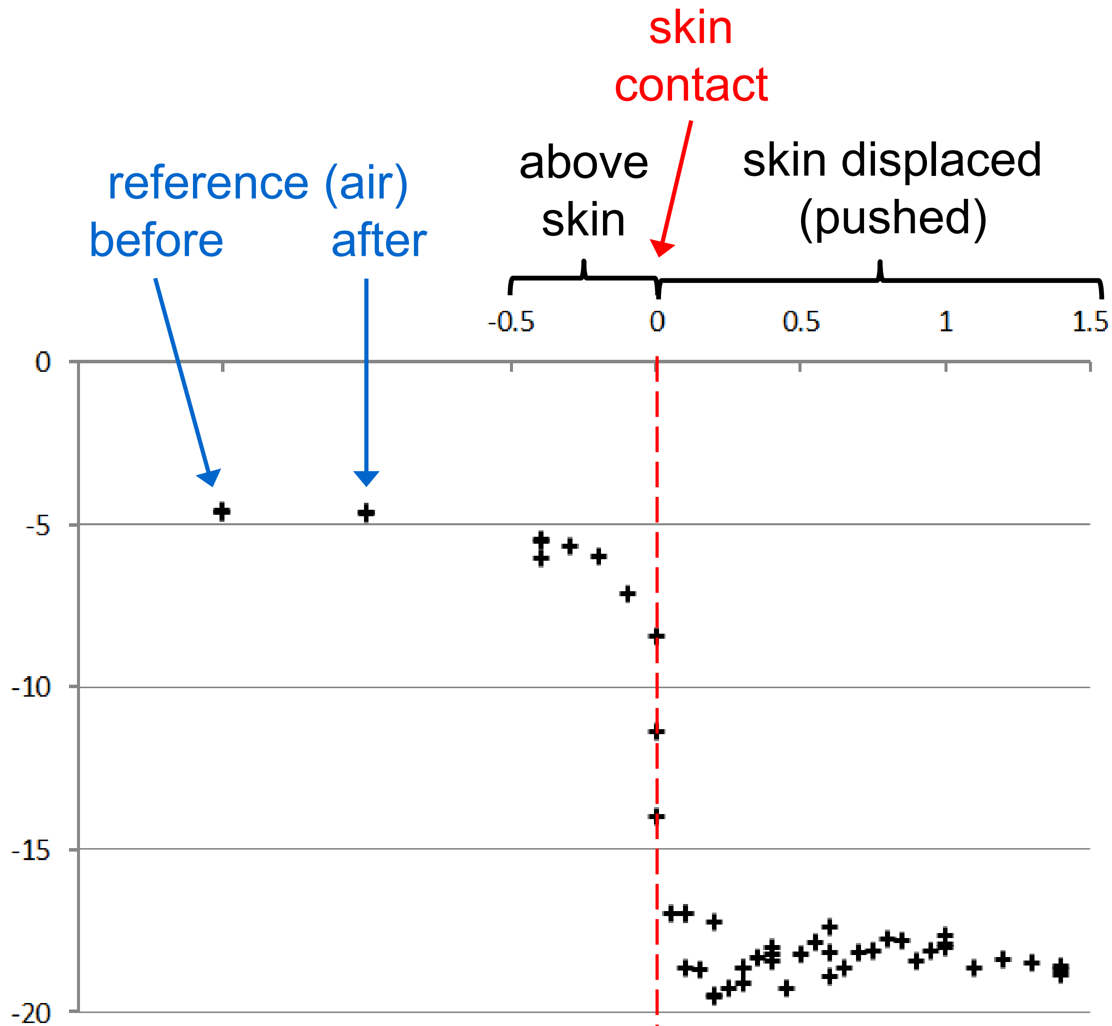
- **Reference measurements:** TEWL dermatological instrument (Khazaka TM300)



Probe pressure operator independency

- stable signal after skin displacement of ~0.1mm

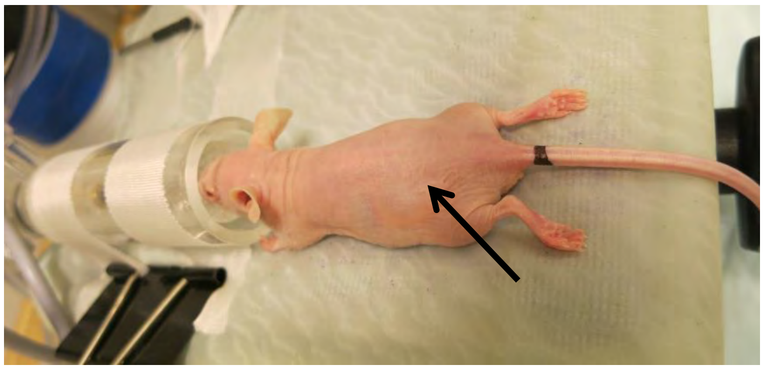




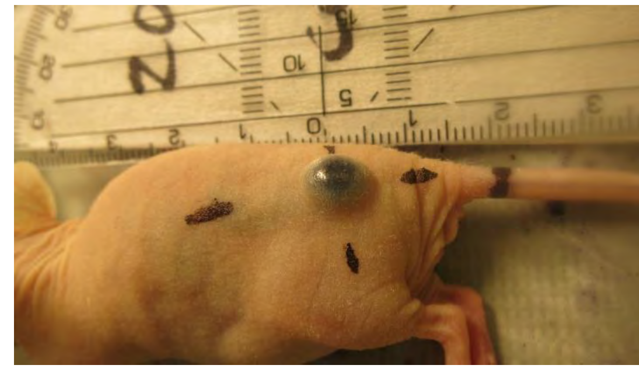
It works – what's next?

Studies on real melanoma.

Murine skin cancer model



12-14 days →

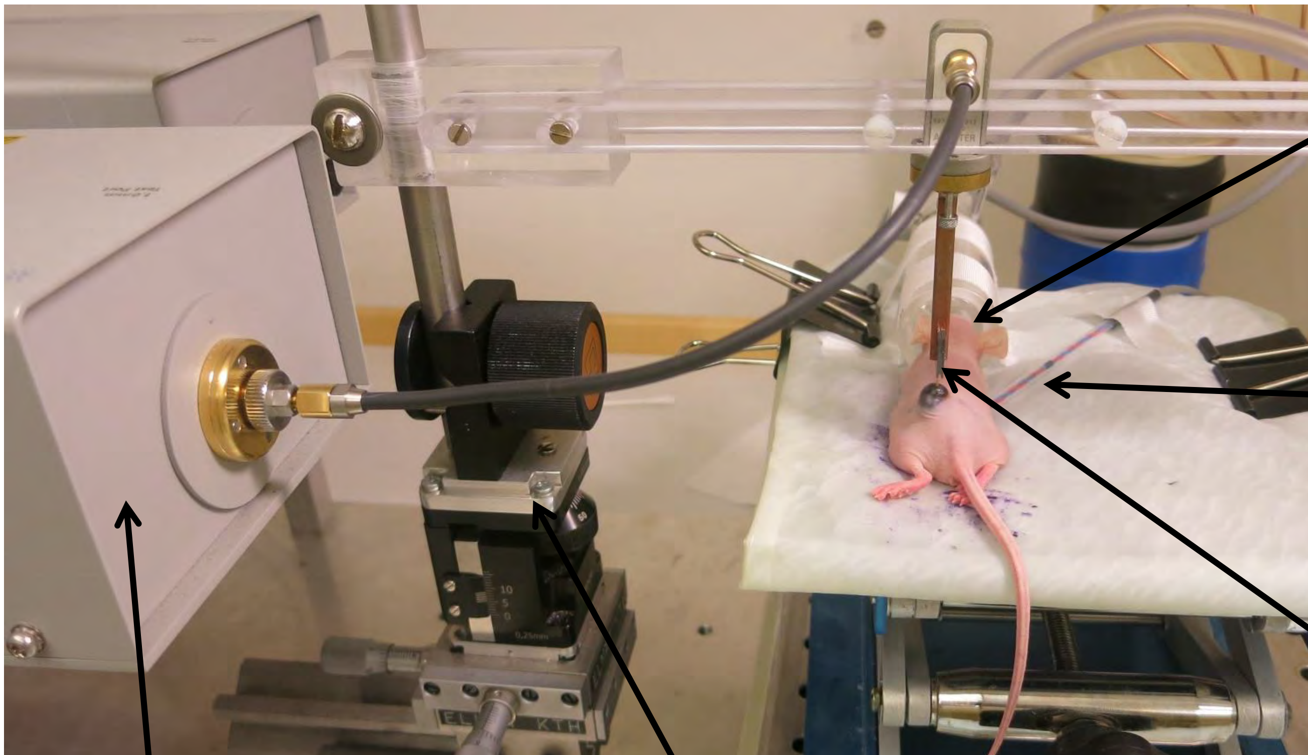


Injection of B16F10 cells

Malignant melanoma tumor

- 6-weeks-old female athymic Nude-Foxn1^{nu} mice
- Subcutaneous injection of 0.5 million 10^6 B16F10 murine melanoma cells in 200 µl PBS
- Palpable tumor of ~1 cm size after 12 – 14 days → termination

Measurement setup



Mouse anesthetized during measurement

Heating mat and temperature sensor for stable mouse body temperature

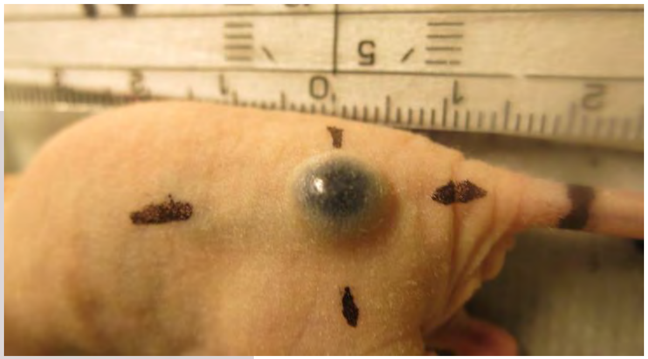
Millimeter-wave probe

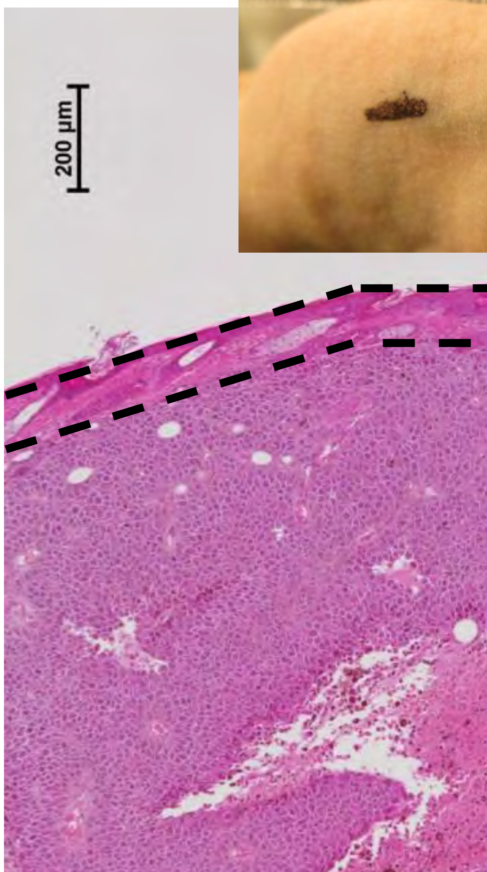
VNA

x-y-z stage to move probe

Results: Histology

Mouse 1

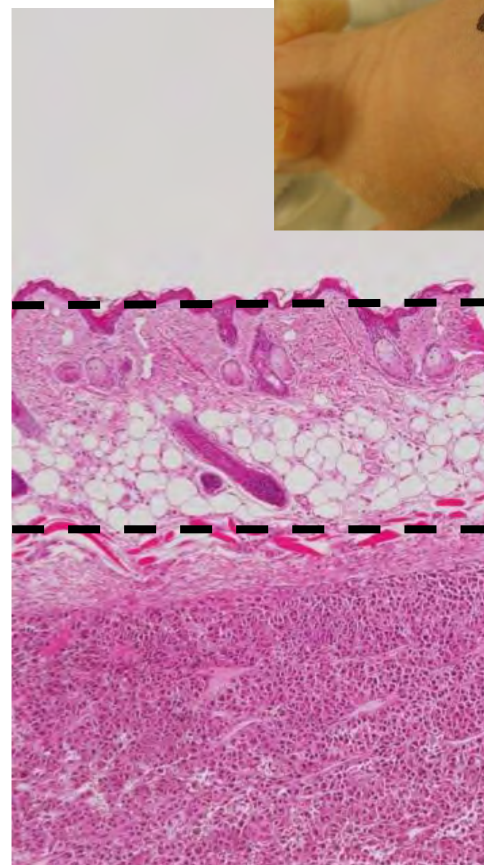




Skin layer ~100 µm

Tumor

Mouse 2



Skin and fat layer ~600 µm

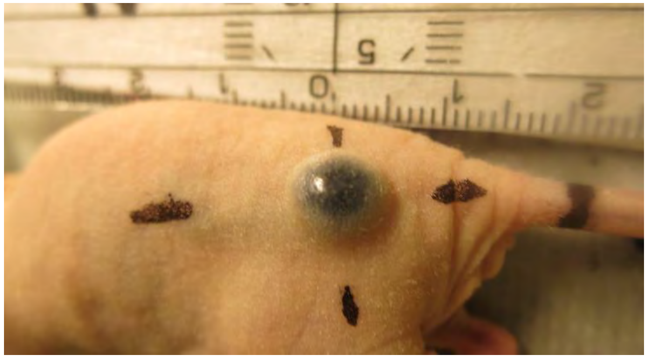
Tumor

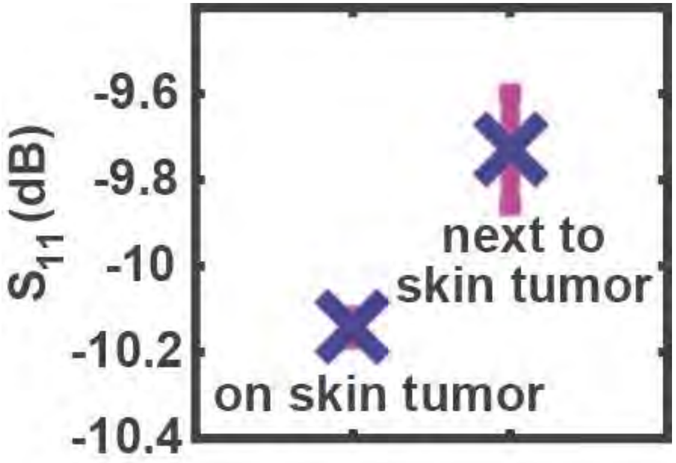
- Tumor inside skin
- represents **realistic** skin tumor

- Tumor beneath skin and fat
- **not** representing skin cancer

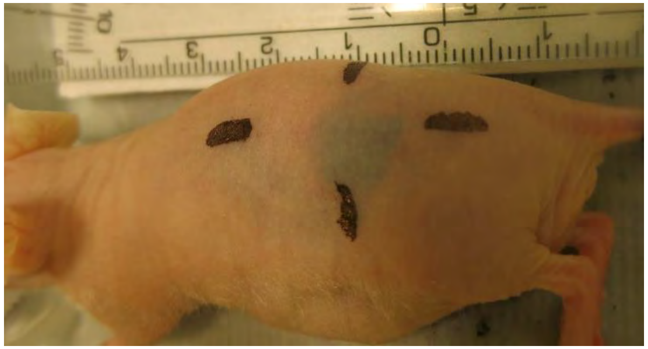
Murine skin cancer model

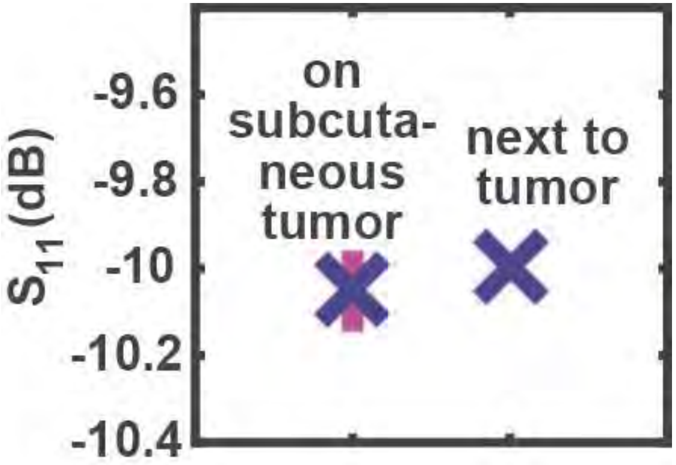
Mouse 1: Tumor inside skin
(represents **realistic** skin tumor)





Mouse 2: Tumor beneath skin
(**not** representing skin cancer)





- ➢ Clear difference in S_{11} between the realistic tumor and the surrounding tissue (6.7 times the average stand. deviations on the same spot)

Acknowledgements

Ethical approvals by Regional Research Ethics Board Stockholm, fulfilling requirements according to the Swedish Ethical Review Act of 2003-06-03 (SFS no 2003:460):

- N80/15 (2014)
- N100/16 (2016)

Funding provided by VINNOVA – Swedish Governmental Agency for Innovation Systems

Conclusions

- microwave interaction with tissue exists and can be used for medical diagnosis
- millimeter and submillimeter-wave frequencies offer many opportunities in medical diagnosis
- a tailor-made, micromachined 100 GHz near-field probe for skin cancer diagnosis was designed and implemented
- successfully characterized was carried out technically and in-vivo, on human and animal models
- the senseor is clearly able to discriminate melanoma from healthy tissue at the targeted tissue depth