A micromachined millimeter-wave skin cancer sensor: from technology development to clinical studies

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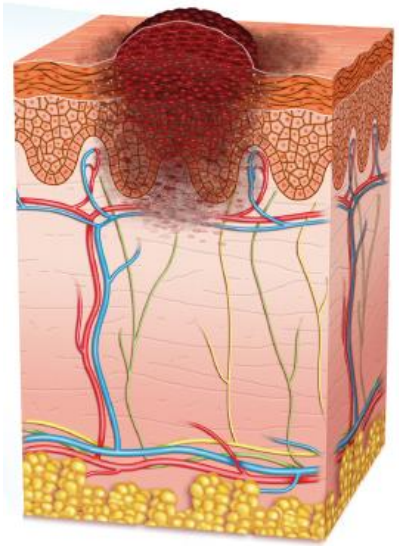
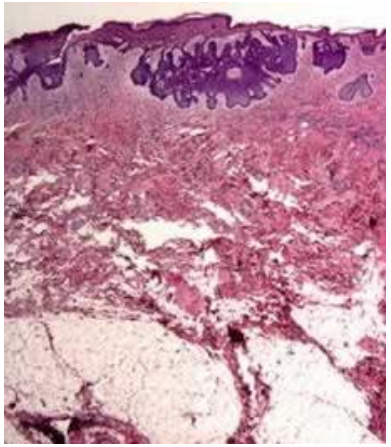
Outline

1. Medical diagnostic tools: opportunities for microwaves
2. Microwave properties of tissue
3. Skin modelling
4. KTH's Micromachined millimeter-wave probe
5. In-vivo studies
6. Conclusions

Part 1. Medical diagnostic tools: opportunities for microwaves

Need for skin-cancer diagnostic tools





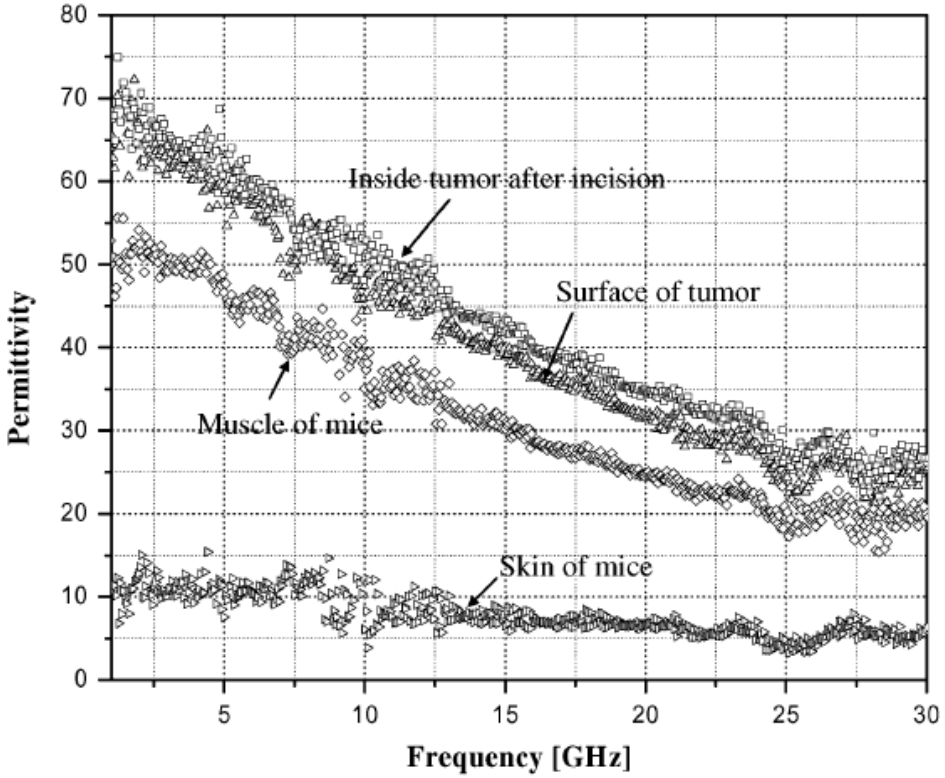
- Skin cancer: most common cancer (for white population)
- Malignant melanoma: by far the deadliest skin cancer
  - >75,000 cases of malignant melanoma in the USA yearly
  - >12,000 deaths from melanoma in the USA yearly
  - highly metastastic, no. 1 cancer killer age adults < 40 years of age
  - high mortality 15-20% for late-stage diagnosis
  - high survival rates (>95% 5y) if early diagnosed
- Highest increase among all cancer types
  - avg. increase of 3-6% each year during last 3 decades
  - 50% increase in mortality since 1973
- Huge screening effort needed to find skin cancer
  - 50-250 screenings for finding 1 melanoma
- Diagnosis only done by highly trained dermatologists
  - High costs for the public healthcare system
  - Delay in diagnosis => higher mortality rate
- Currently no established sensor technology available

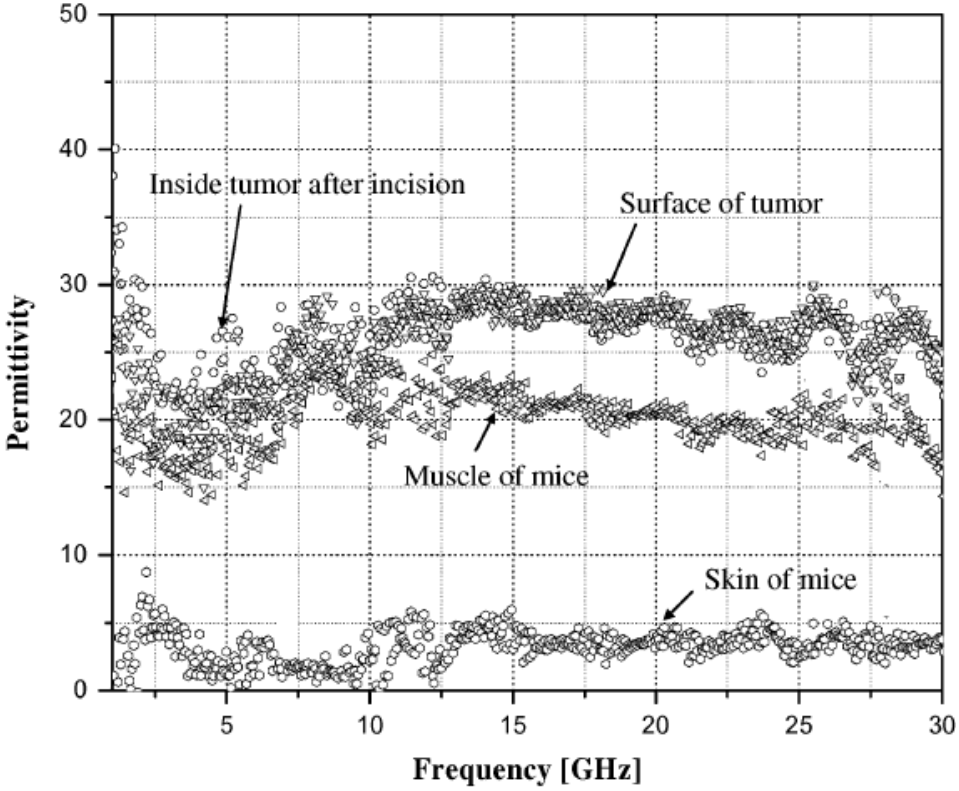
Microwave cancer diagnosis

- 1926: first study on breast cancer tissue: significantly different permittivity than healthy tissue (20kHz)
- below 30MHz, differences are based on differences of intracellular membranes of cancer (first study 1946): impedance measurements
- above 1GHz, energy absorption is significantly higher in malignant tumors, attributed to increased free and bound water content of fast and uncontrolled growing tissue
- most tumors 10-20% difference in permittivity to healthy tissue
- breast tumors: factor ×2 higher discrimination

Cancer Res., vol. 6, pp. 574/577, 1946.
European Urology 47 (2005) 29–37.
Phys Med Biol 1980;25:1149.

Healthy vs. cancer tissue at microwave frequencies





KIM *et al.*: *IN VITRO* AND *IN VIVO* MEASUREMENT FOR BIOLOGICAL APPLICATIONS USING MICROMACHINED PROBE
IEEE TRANSACTIONS ON MICROWAVE THEORY AND TECHNIQUES, VOL. 53, NO. 11, NOVEMBER 2005

Healthy vs. cancer tissue at submillimeter-wave frequencies

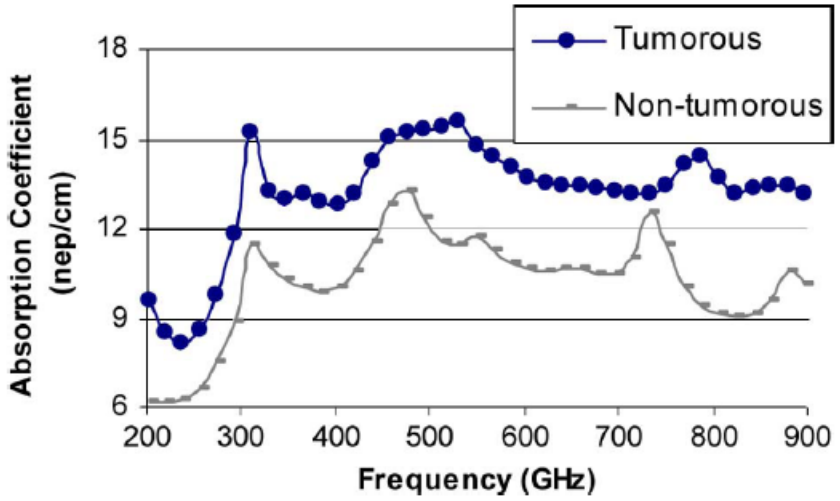


Fig. 5. Absorption coefficients of tumorous and nontumorous tissues from 200 to 900 GHz are shown. Peaks can be observed at 311, 460, 732, and 787 GHz (from [33]).

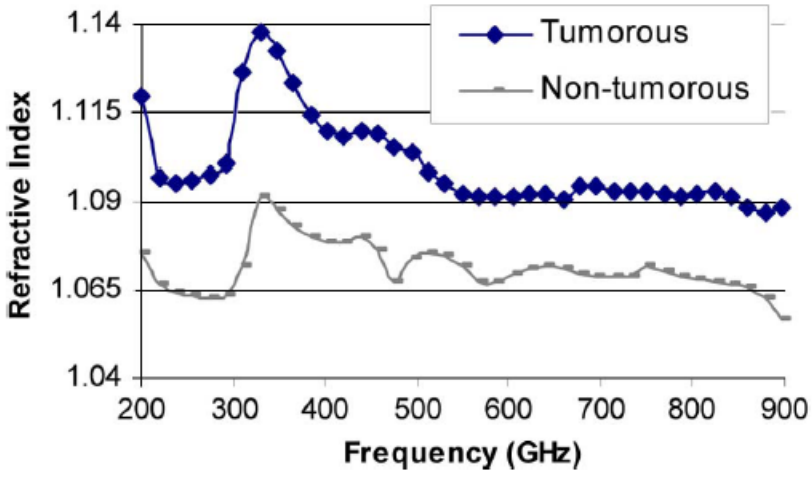


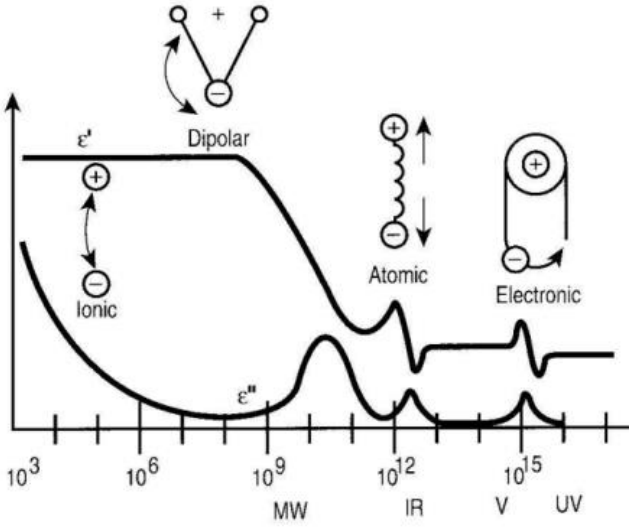
Fig. 6. Refractive indices of tumorous and nontumorous tissues from 200 to 900 GHz are plotted. Peaks can be observed at 329 GHz and a dip at 476 GHz for nonmalignant tissues (from [33]).

KHAN *et al.*: BROADBAND DIELECTRIC CHARACTERIZATION OF TUMOROUS AND NONTUMOROUS BREAST TISSUES
IEEE TRANSACTIONS ON MICROWAVE THEORY AND TECHNIQUES, VOL. 55, NO. 12, DECEMBER 2007

Part 2. Microwave properties of tissue

Modelling of tissue permittivity

- Loss mechanism in tissue: Permittivity dispersion from water-molecule polarization:
  - free water molecules
  - motionally restricted water molecules
- Multiple relaxation mechanisms happen at different frequencies



- modeling of relaxation regions by single relaxation time constants:

$$\hat{\varepsilon} = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1 + j\omega\tau}$$

Debye expression for a single region

- modelling of multiple regions => multi-pole models

Multi-pole models

- **Debye model**: $$\epsilon(\omega)_D = \epsilon_\infty + \sum_{m=1}^{n} \frac{\Delta\epsilon_m}{1 + i\omega\tau_m} + \frac{\sigma}{i\omega\epsilon_0}$$ static ionic conductivity term

- complexity of biological material => broadening of different dispersion regions => modified Debye model =>
- **Cole-Cole model**:

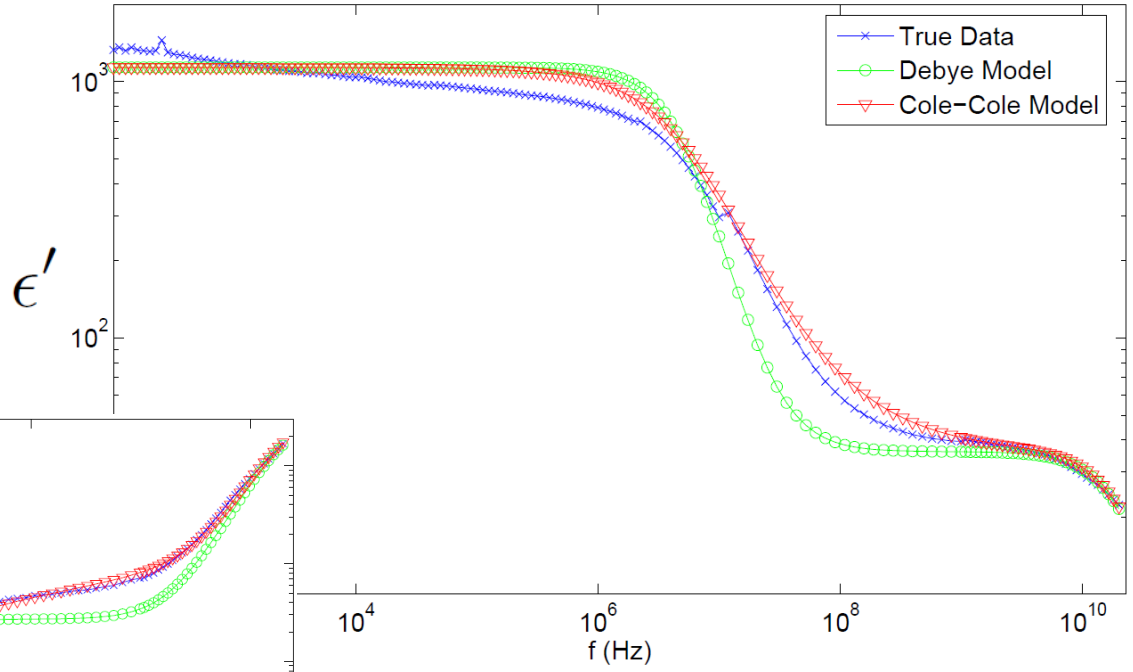
$$\epsilon(\omega)_{CC} = \epsilon_\infty + \sum_{m=1}^{n} \frac{\Delta\epsilon_m}{1 + (i\omega\tau_m)^{(1-\alpha_m)}} + \frac{\sigma}{i\omega\epsilon_0}$$

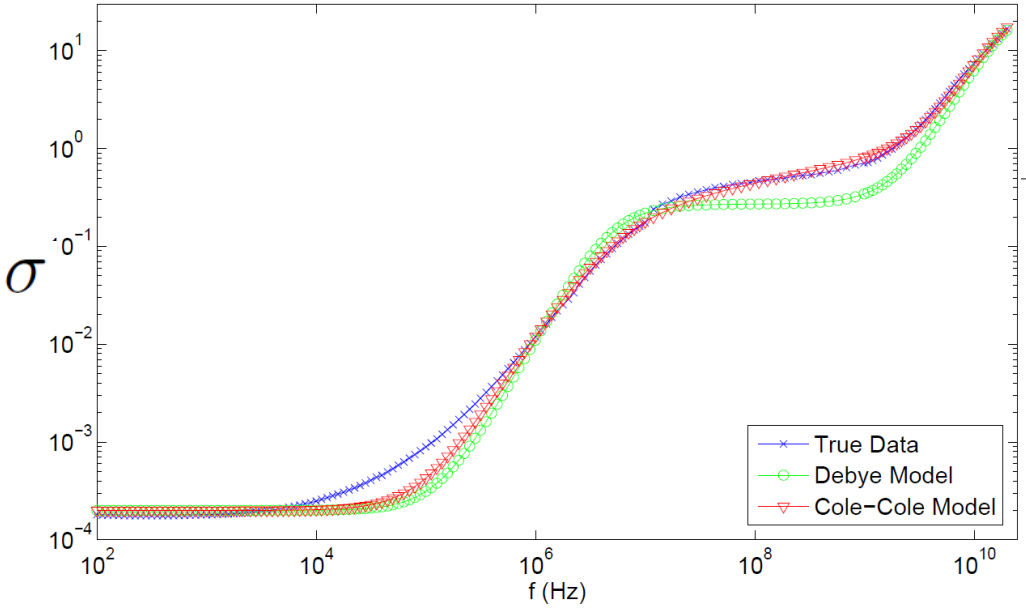
- Complex permittivity:

$$\epsilon = \epsilon' - \mathrm{i}\epsilon'' \qquad \epsilon'' = \frac{\sigma}{\epsilon_0\omega} \qquad \sigma = \frac{1}{\rho}$$

”The dielectric properties of biological tissues: III.”, Phys Med Biol 41 (1996) 2271-2293

Model comparison: data fitting





Data from: Nathan Gibson, Oregon State Univ.

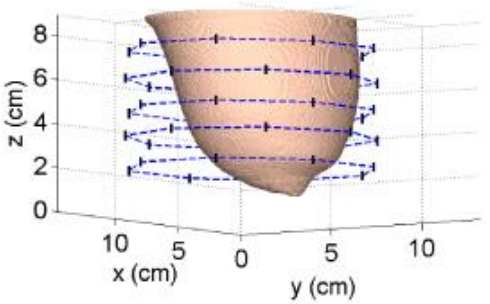
Parameters for tissue types

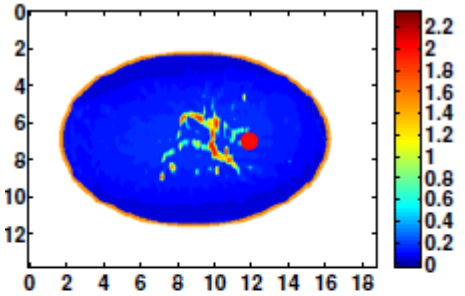
- Single-term Debye model

$$\varepsilon_c(\omega, \epsilon_s, \epsilon_\infty, \sigma_s, \tau) = \epsilon_\infty + \frac{\epsilon_s - \epsilon_\infty}{1 + j\omega\tau} + \frac{\sigma_s}{j\omega\epsilon_0}$$

- Parameters for numerical breast model:

Material (percentile)	ε_s	ε_∞	σ_s (S/m)
Safflower oil	2.93	2.21	0.0120
Adipose tissue (min)	2.42	2.28	0.0023
Adipose tissue (25th)	4.07	2.74	0.0207
Adipose tissue (50th)	4.81	3.11	0.0367
Adipose tissue (75th)	7.62	4.09	0.0842
Fibroglandular tissue (25th)	36.7	16.8	0.461
Fibroglandular tissue (50th)	49.1	17.5	0.720
Fibroglandular tissue (75th)	54.3	18.6	0.817
Fibroglandular tissue (max)	67.2	29.1	1.38
Malignant			
Endogenous	56.6	18.8	0.803
With μ-bubbles	39.7	13.2	0.562
With nanotubes	69.3	14.8	1.47
Skin	40.1	15.3	0.74





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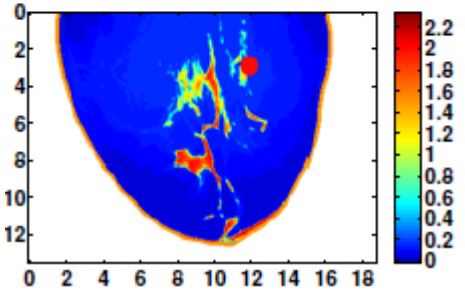


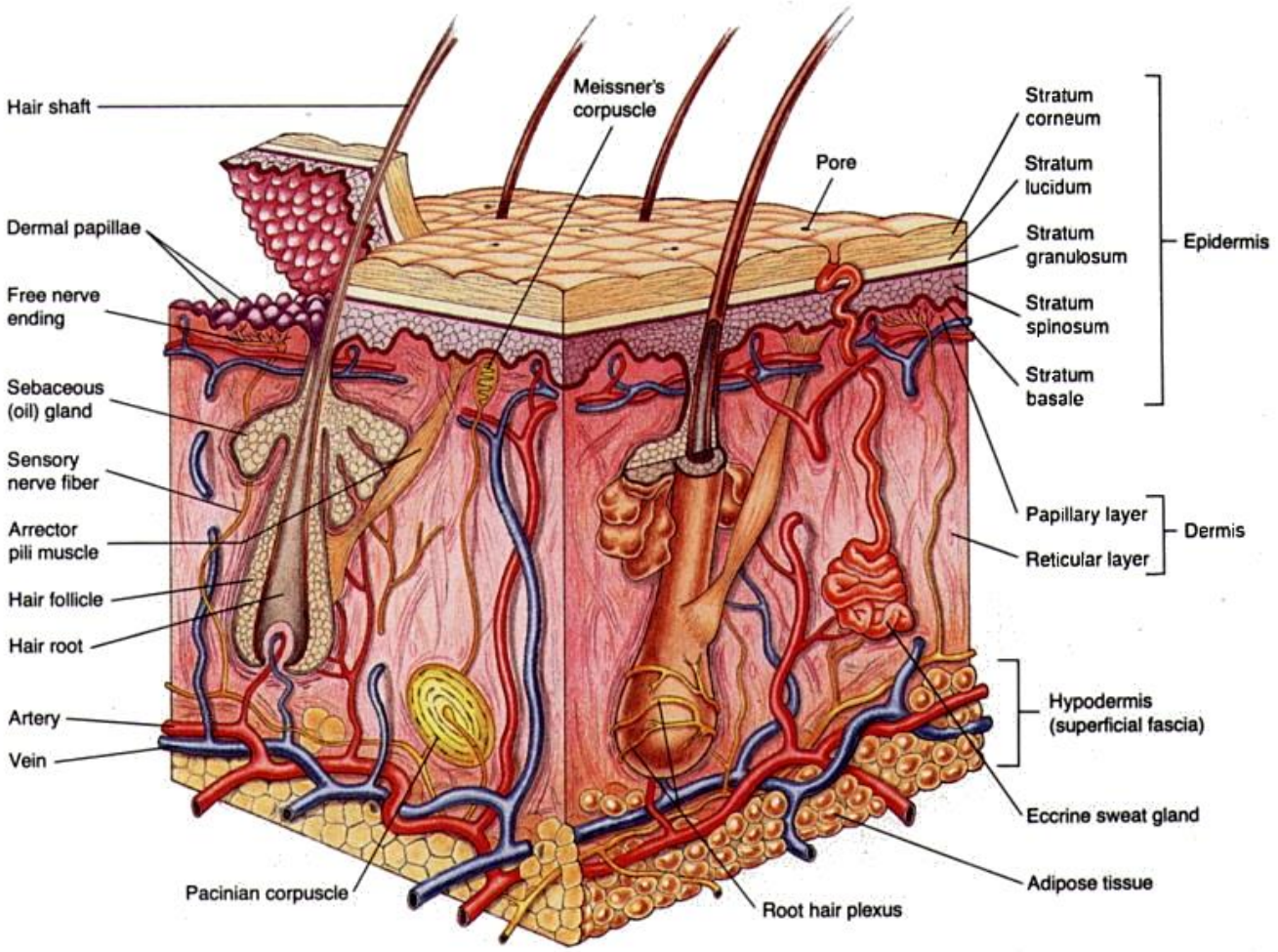
τ = 15 ps
0.5-20 GHz

"A TSVD Analysis of Microwave Inverse Scattering for Breast Imaging" J D Shea*, B D Van Veen, S C Hagness (Univ. Wisconsin)

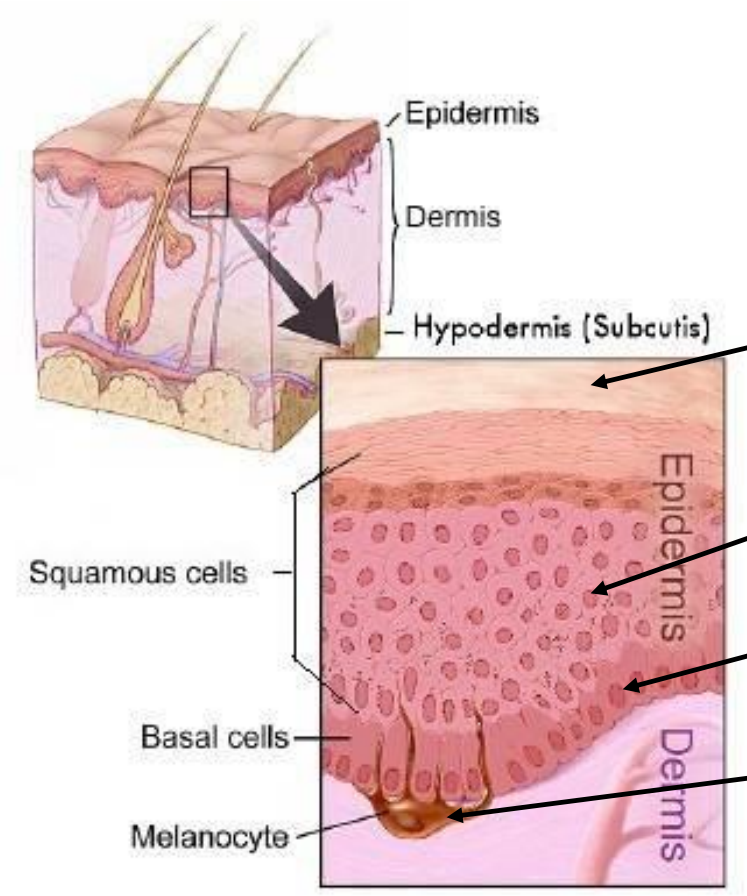
Part 3. Modelling of skin

Modelling of skin ...

for the dermatologist, skin tissue is very complex, inhomogeneous and different on different body positions



The epidermis, the origin of skin cancer



stratum corneum (dead keratinocytes)

origin of squamous cell carcinoma

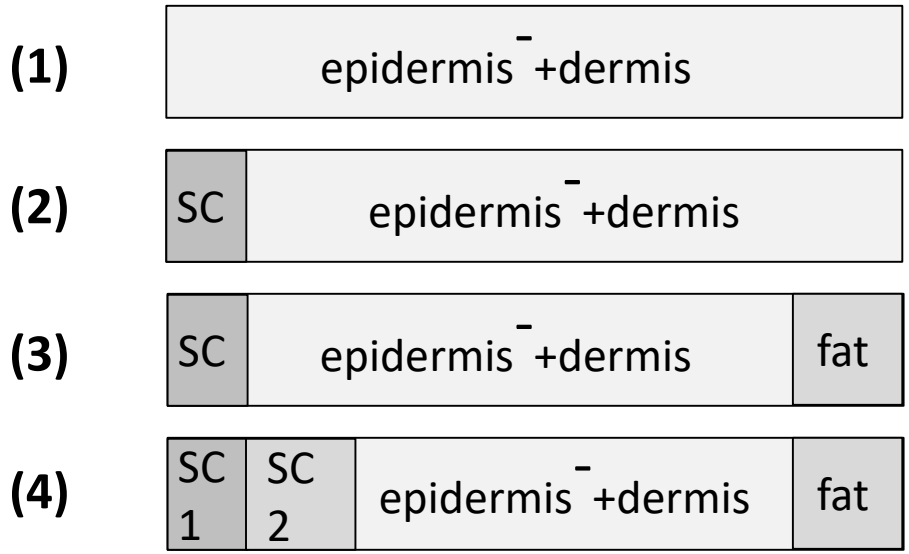
origin of basal cell carcinoma

origin of melanoma

Epidermis: 0.007-0.700 mm thick

Epithelial tissue in the body is the origin for 80% of all cancers

Microwave models of multi-layer skin



Model 1: homogeneous skin (65-70% water)

Model 2: stratum corneum (30-43% water) on homogeneous skin

Model 3: stratum corneum on homogeneous skin + underlying fat layer

Model 4: 2-layer (thick) stratum corneum and underlying fat layer

		Forearm model number			Palm model number		
	Parameter	1	2	3	2	3	4
SC	ϵ_∞	—	2.96	2.96	3.63	3.63	3.63; 3.63
	$\Delta\epsilon$	—	—	—	9.7	9.5	10.1; 0.0
	d, mm	—	0.015	0.015	0.43	0.42	0.43; 0.05
	σ, S/m	—	0	0	0	0	0
E^-+D	ϵ_∞	4.0	4.0	4.0	4.52	4.52	4.52
	$\Delta\epsilon$	32.0	32.6	32.4	27.2	26.4	27.2
	d, mm	—	—	1.45	—	1.85	1.8
	σ, S/m	1.4	1.4	1.4	1.4	1.4	1.4
	$\tau \times 10^{12}$, s[a]	6.9	6.9	6.9	6.9	6.9	6.9

epidermis ... epidermis without stratum corneum

SC ... stratum corneum

Bioelectromagnetics 28:331–339 (2007)

Part 4. A micromachined high-resolution millimeter-wave probe

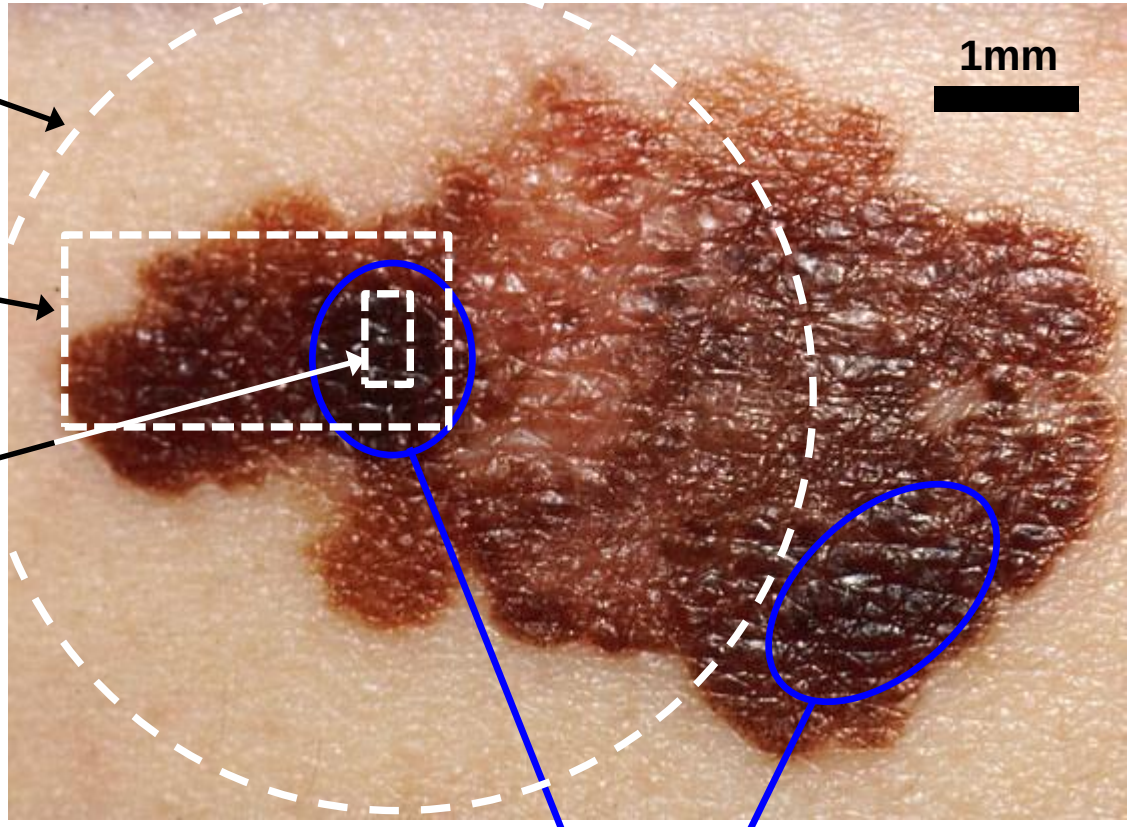
Why high resolution?

conventional RF probe size (5mm diameter)

millimeter-wave probe (2.5x1.3mm)

micromachined millimeter-wave probe (0.6x0.3mm)

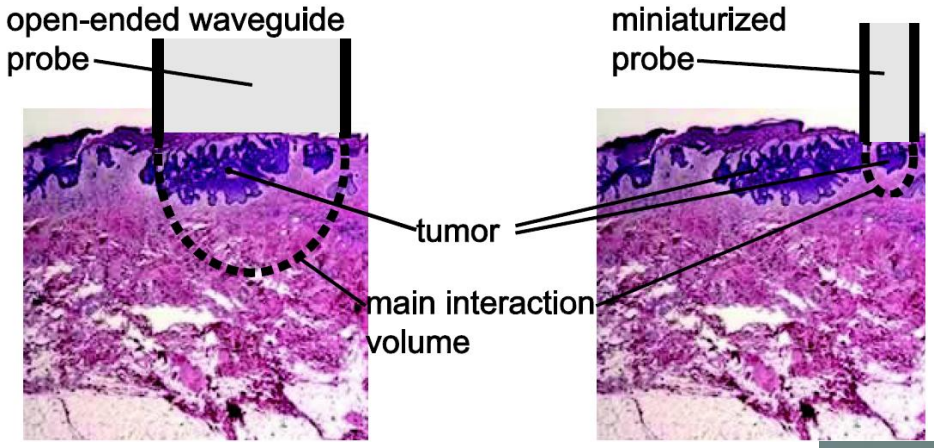
- 0.9% of size of RF probe
- 5.6% of size of mmW probe



High-resolution probe tip is important for high responsivity over surrounding healthy tissue

malign melanoma speckles in >5mm benign tumor

Optimum microwave interaction volume



- limiting main interaction volume to <1mm depth
- melanoma growth >1mm => metastases

- small probe tip: => high lateral resolution
- small tip + high frequency: => limited pentration depth
- high frequency (100GHz): high responsivity for small probe tip