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

Fritzi Töpfer¹, Lennart Emtestam², Joachim Oberhammer¹

1  KTH Royal Institute of Technology – School of Electrical Engineering  
   100 44 Stockholm, Sweden  joachimo@kth.se
2  Karolinska Institutet, Dept of Dermatology, Solna, Stockholm, Sweden
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 metastatic, 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.

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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]).
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

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Multi-pole models

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

- 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:**
  \[
  \epsilon = \epsilon' - i\epsilon'' \quad \epsilon'' = \frac{\sigma}{\epsilon_0\omega} \quad \sigma = \frac{1}{\rho}
  \]


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Model comparison: data fitting

Data from: Nathan Gibson, Oregon State Univ.
Parameters for tissue types

• Single-term Debye model

\[ \varepsilon_c(\omega, \varepsilon_s, \varepsilon_{\infty}, \sigma_s, \tau) = \varepsilon_{\infty} + \frac{\varepsilon_s - \varepsilon_{\infty}}{1 + j\omega\tau} + \frac{\sigma_s}{j\omega\varepsilon_0} \]

• Parameters for numerical breast model:

<table>
<thead>
<tr>
<th>Material (percentile)</th>
<th>( \varepsilon_s )</th>
<th>( \varepsilon_{\infty} )</th>
<th>( \sigma_s ) (S/m)</th>
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<tr>
<td>Safflower oil</td>
<td>2.93</td>
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<td>Adipose tissue (min)</td>
<td>2.42</td>
<td>2.28</td>
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<td>Adipose tissue (25th)</td>
<td>4.07</td>
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<td>Adipose tissue (75th)</td>
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<td>Fibroglandular tissue (25th)</td>
<td>36.7</td>
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<td>49.1</td>
<td>17.5</td>
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<td>Fibroglandular tissue (75th)</td>
<td>54.3</td>
<td>18.6</td>
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<td>Fibroglandular tissue (max)</td>
<td>67.2</td>
<td>29.1</td>
<td>1.38</td>
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<tr>
<td>Malignant</td>
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<tr>
<td>Endogenous</td>
<td>56.6</td>
<td>18.8</td>
<td>0.803</td>
</tr>
<tr>
<td>With ( \mu )-bubbles</td>
<td>39.7</td>
<td>13.2</td>
<td>0.562</td>
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<tr>
<td>With nanotubes</td>
<td>69.3</td>
<td>14.8</td>
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<td>Skin</td>
<td>40.1</td>
<td>15.3</td>
<td>0.74</td>
</tr>
</tbody>
</table>

\( \tau = 15 \text{ ps} \)

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
for the dermatologist, skin tissue is very complex, inhomogeneous and different on different body positions
The epidermis, the origin of skin cancer

Epidermis: 0.007-0.700 mm thick

- stratum corneum (dead keratinocytes)
- origin of squamous cell carcinoma
- origin of basal cell carcinoma
- origin of melanoma

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

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Microwave models of multi-layer skin

1. **Model 1:** homogeneous skin (65-70% water)
   - epidermis + dermis

2. **Model 2:** stratum corneum (30-43% water) on homogeneous skin
   - SC epidermis + dermis

3. **Model 3:** stratum corneum on homogeneous skin + underlying fat layer
   - SC epidermis + dermis

4. **Model 4:** 2-layer (thick) stratum corneum and underlying fat layer
   - SC1 epidermis + dermis
   - SC2 fat

<table>
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<th>Palm model number</th>
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<td>$\Delta\epsilon$</td>
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<td>—</td>
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<td>$d$, mm</td>
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<td>$\sigma$, S/m</td>
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<td>—</td>
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<td>$\tau \times 10^{12}$, s</td>
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</table>

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Part 4. A micromachined high-resolution millimeter-wave probe
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 penetration depth
- high frequency (100GHz): high responsivity for small probe tip

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