RF Applications in Healthcare: Overview of activities in CTR

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Main Applications

• **Microwave medical imaging**
  - Use radio waves to create medical diagnostic devices
  - Expertise in imaging algorithms and computational EM
  - Current work on hardware and experimental testbeds
  - Interdisciplinary work with KLC’s IPS on nanoparticles for microwaves

• **Non-invasive glucose monitoring**
  - Joint R&D work with industry
  - Emphasis on hardware, measurements, first clinical trials
  - New science on impedance-matching surfaces

• **Other activities**
  - Antenna design for telemetry and on-body communications
  - Theoretical models for sensing and communications at nanoscale
Microwave Medical Imaging (MWI)

• Why?
  • Safe (non-ionizing radiation)
  • Easy exams for patients and clinicians
  • Low cost and improved hardware (RF/telecoms industries)

• How?
  • The object is illuminated with EM waves
  • The scattered signals are received by the surrounding antennas
  • An image formation algorithm is invoked
  • The received information is translated into an image

• Can it work?
  • Is there enough contrast in human tissues?
  • Resolution vs. penetration depth
The Breast Cancer Problem

- How to combat breast cancer?
  - Healthy lifestyle
  - Early detection and treatment

Source: Cancer research UK, futuretimesline.net
Breast Cancer Diagnosis

Existing Techniques

X-Ray
Mammography

Microwave Imaging: Attractive alternative
(research since mid 90s)
Existing Experimental Setups


Towards a System that Builds on Research and Innovative Design

How do we integrate the sophisticated imaging algorithms with hardware and innovative design?

Mediwise and KCL
Dielectric Properties of Tissues

- Large-scale studies of UWB microwave dielectric properties of normal, benign, and malignant breast tissues
    - vol. 52, pp. 6093-6115, 2007

- Dielectric contrast
  - Malignant vs. fatty tissues: ~10:1
  - Malignant vs. fibroglandular: ~10%.
  - Malignant tissue properties range overlaps fibroglandular range
Penetration Depth in Skin and Fat Tissues at Microwave Frequencies

Frequency (GHz)

Penetration Depth (m)

Skin
Fat
Microwave Imaging (MWI)


Microwave Tomography

Iterative inverse scattering algorithms

- Complete dielectric profile of the breast is reconstructed based on antenna-received signals.
- Computationally demanding → need for efficient forward solvers and inversion algorithms
- Typical inverse scattering challenges: Non-uniqueness, ill-posedness, robustness

Approaches: Newton-based, Level Sets, Contrast Source Inversion, Conjugate Gradient Time-Domain methods
Forward Solvers: The Finite Difference Time Domain (FDTD) Method

- FDTD is a numerical analysis technique used for modeling computational electrodynamics.
- In 1966, Yee described the FDTD for solving Maxwell’s curl equations on grids staggered in space and time.
- We apply the FDTD as a forward solver for simulating the electromagnetic field of breast model.

Illustration of a standard Cartesian Yee cell used for FDTD, about which electric and magnetic field vector components are distributed.
EM Inverse Scattering within the DBIM Method

- Make linear approximation (distorted-Born iterative method)
  \[ E_s(r_n, r_m) = E(r_n, r_m) - E_b(r_n, r_m) \]
  \[ = \omega^2 \mu \int_V G_b(r_n, r) E(r, r_m)(\epsilon(r) - \epsilon_b(r)) dr \]

- Simplify Green function
  \[ G_b(r_n, r) = \frac{i}{\omega \mu} E_b(r, r_n) \]

- Solve the non-linear problem iteratively
  \[ \epsilon_{b_i+1} = \epsilon_{b_i} + \hat{O}_{i+1} \]

- Discretize integral equation
  \[ E_s(r_n, r_m) \approx i \omega \int_V E_b(r, r_m) E_b(r, r_n) O(r) dr \]

\[ b(\omega) = A(\omega) o. \]
EM Inverse Scattering within the DBIM

- Guess Initial Profile, \( \varepsilon^b \)
- Compute Fields, \( E^b \) & Green’s Fn, \( G^b \) (Forward Solution)
- Discretize Integral Equations
- Solve Linear System (Inverse Solution)
- Add Solution to Estimate

\[ E(r) - E^b(r) = \int_V dr' \overline{G}^b (r, r') O(r') E^b(r') \]
How can we improve these images?

Guess Initial Profile, $\varepsilon^b$

Compute Fields, $E^b$ & Green’s Fn, $G^b$ (Forward Solution)

Discretize Integral Equations

Solve Linear System (Inverse Solution)

Add Solution to Estimate

Multi-Frequency Linear Inverse Problem

\[ A\delta_{\varepsilon} = E^S \iff \begin{bmatrix} \cdots & \omega^2 \mu G^b(\vec{r}_n, \vec{r}_m) E^b(\vec{r}_n) \cdots \end{bmatrix} \begin{bmatrix} \varepsilon(\vec{r}) - \varepsilon^b(\vec{r}) \end{bmatrix} = \begin{bmatrix} E^m(\vec{r}_n) - E^b(\vec{r}_n) \end{bmatrix} \]

\[ \epsilon_r(\omega) = \epsilon_{\infty} + \frac{\Delta \epsilon}{1 + j\omega\tau} + \frac{\sigma_s}{j\omega\epsilon_{\infty}} \]

\[ \begin{bmatrix} \Re \{ A(\omega) \} & \Re \{ \epsilon_{\Delta}(\omega) A(\omega) \} & \Re \{ \epsilon_{\sigma}(\omega) A(\omega) \} \\ \Im \{ A(\omega) \} & \Im \{ \epsilon_{\Delta}(\omega) A(\omega) \} & \Im \{ \epsilon_{\sigma}(\omega) A(\omega) \} \\ \vdots & \vdots & \vdots \end{bmatrix} \begin{bmatrix} \delta_{\varepsilon, \omega} \\ \delta_{\Delta, \omega} \\ \delta_{\sigma, \omega} \end{bmatrix} = \begin{bmatrix} \Re \{ E^S(\omega) \} \\ \Im \{ E^S(\omega) \} \\ \vdots \end{bmatrix} \]

\[ \Delta E_s(\vec{r}_T, \vec{r}_R) = E(\vec{r}_T, \vec{r}_R) - E^b(\vec{r}_T, \vec{r}_R) = \]

\[ = \omega^2 \mu \int_V G^b(\vec{r}, \vec{r}_R) \Delta \chi(\vec{r}) E^b(\vec{r}, \vec{r}_T) d\vec{r} = \mathcal{L}^b [\Delta \chi] \]
Regularization by Projection (with CNR-IREA)

Sparsity-based Approach (with Sharif University)

L2-SAT Improvement (with Sharif University)

- L2-SAT iterate:
  \[ x^{k+1} = T^k \left( (1 - 2\lambda_2) x^k + \mu \left( A^T (y - Ax^k) - \lambda_1 h(x^k) \right) \right) \]

- Further improvement in convergence/computational complexity

- Enhanced Resolution Images

The DBIM/TwIST Algorithm

- Relative to conventional iterative shrinkage/thresholding (IST) algorithms, the TwIST exhibits much faster convergence rate and robustness.

\[ \Delta \chi_{k+1} = (1 - \alpha) \Delta \chi_{k-1} + (\alpha - \beta) \Delta \chi_k + \beta \Psi_\lambda (\Delta \chi_k + \Lambda^* (y - \Lambda \Delta \chi_k)) \]

How well can we do in terms of resolution?

Reconstruction of a 0.5 mm MRI-based model

**Known skin**

**Unknown skin**
Development of a Lab Prototype

The MWI system comprised of circular array of antennas being developed by KCL/MediWiSe is shown below.

The envisioned MWI system

The simulation set up of a MWI system
Antenna Array Comparisons

4-element array of custom-designed antennas in immersion liquid

4-element array of printed V-antennas (Chalmers)

4-element array of monopoles (Dartmouth)
Work with KCL’s IPS on NPs as Contrast Agents

Our current BBSRC-funded PhD project investigates the effect of various nanoparticles on microwave properties.

Fig 1a: Relative permittivity of Compound 1 in water measured from 0.5 to 20GHz

Fig 1b: Relative permittivity of Compound 1 in Glycerol: Water (3:2) measured from 0.5 to 20GHz
Non-invasive Glucose Monitoring

- Insulin: controls glucose absorption
- Diabetes: lacking ability to control insulin
- Threats: vascular complications in the eyes, nervous system, kidneys and heart.
- Europe is spending €90 billion/year

Monitoring Glucose as a Type 1 Patient

- Recommended: 8-10 readings per day
- Average: 5 readings per day
- Invasive glucose monitoring cost: approx. €1,000 per year
GlucoWise Platform (www.mediwise.co.uk)

Pain-free Sensor

Mobile App

Smart Cloud

1st and 2nd round of experiments

Clinical trials

Device Launch

2013

2014

2015

2016

2017

2018

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First Experimental Setup

- Two V-band waveguides with a sample between them
- Tank holding the solutions
Simulation of the Experiment

- To validate the experimental results a set of simulation was performed.

Experiment

Simulation

Prepared samples
Main Results

Transmission coefficients at 72.4 GHz (one of the frequencies with higher sensitivity)

Simulations and Experiment Comparison

Final (Miniaturized) System: Antenna Design

- S-Parameter [Magnitude in dB]
  - Frequency / GHz
  - $S_{11}$

- Farfield (Array) Gain Abs (Phi=90)
  - Frequency = 60
  - Main lobe magnitude = 13.5 dB
  - Main lobe direction = 1.0 deg.
  - Angular width (3 dB) = 36.6 deg.
  - Side lobe level = -11.1 dB

- Farfield (Array) enabled (W.R. > 1)
  - Farfield (f=60) [1]
  - Abs
  - Gain
  - Frequency = 60
  - Rad. effic. = -0.1530 dB
  - Tot. effic. = -0.1620 dB
  - Gain = 13.00 dB

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Next-Generation Experimental System
Novel Science for Skin Impedance Matching

- Important Problem: Impedance mismatch between air and skin
- Suggested Solution: An impedance-matching metamaterial is added between the skin and the sensor to enhance signal penetration.
Predicted Metamaterial (MM) Performance

Power Absorbed in Tissue (W)

Frequency (GHz)

- Tissue
- Metamaterial and Tissue

57%
MM performance for different angles of incidence

- This simulation was done to study the metamaterial performance when the plane wave does not have a normal incidence.

- The changes in the angle of incidence produce differences up to 38.12 dB in $S_{11}$ and 9.04 dB in the $S_{21}$ at 60 GHz.
Novel Antennas in the MICS, ISM and UWB band

Novel antennas designed, studied, and optimized using CST software

- Considerations: simplicity, size, gain, efficiency, SAR values
- CSTS software allows very accurate modeling (e.g. realistic feed) and analysis (e.g. calculation of gain and far-field radiation patterns)

Fabrication and experimental validation

- Measurement of return loss and coupling
- Use of VNA and phantoms for the experimental validation
### Novel Antennas in the MICS, ISM and UWB band

<table>
<thead>
<tr>
<th>Antenna Type</th>
<th>Frequency range</th>
<th>Purpose</th>
<th>Antenna size</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>UWB 1</td>
<td>3.2GHz - 6GHz</td>
<td>MWI</td>
<td>16x25mm²</td>
<td>Fabricated &amp; Measured</td>
</tr>
<tr>
<td>UWB2</td>
<td>2.78GHz – 10.9GHz</td>
<td>MWI</td>
<td>16x25mm²</td>
<td>Fabricated &amp; Measured</td>
</tr>
<tr>
<td>UWB3</td>
<td>3.1GHz – 10.6GHz</td>
<td>UWB</td>
<td>37.8 x 39 mm²</td>
<td>Fabricated &amp; Measured</td>
</tr>
<tr>
<td>ISM</td>
<td>2.45GHz</td>
<td>On-body</td>
<td>40x40mm²</td>
<td>Fabricated &amp; Measured</td>
</tr>
</tbody>
</table>
Simulated vs. Measured Return Loss

![Frequency vs. Return Loss Graphs](image)

- **Simulated** vs. **Measured**
- **Frequency [GHz]**: 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 8, 9, 10, 11
- **S11 [dB]**: -5, -10, -15, -20, -25, -30, -35, -40, -45

**Graphs**:

- **Graph 1**: Frequency [GHz] vs. S11 [dB] for various simulated and measured conditions.
- **Graph 2**: Frequency [GHz] vs. S11 [dB] for a specific comparison range.
Communications & Sensing at the Nanoscale (led by Y. Chen)

**Transient Microbot (TM)**

- Sensor
- Propeller
- Steering wheel
- Navigator
- Fuel
- Nanoload

**MTB**

- Injected microbots
- Propelling field
- Loading/injection
- Microbot footprints
- Unloading
- Transmitter
- Channel
- Receiver

Transient electronics
Bioresorbable Transient Electronics
Biodegradable Magnetotactic Bacteria (MTB)

a, b) Microscopy images of MTB targeted in the denser interstitial region of a tumor from the blood vessels

c) Electron microscopy image of one MC-1 MTB

d) Agglomeration of MC-1 MTB being controlled to swim along pre-determined paths in microvasculature, tracked under an optical microscope

e) Various concentrations of MC-1 MTB detected and imaged with MRI
A “Touchcom” Model for Targeted Drug Delivery

- Abstracting the **loading/injection** operation as the **transmitting** process
- Abstracting the **propagation** process as the **channel**, where the transmitted signal is sent via the active transport scheme
- Abstracting the **unloading** operation as the **receiving** process
Propagation of TM Swarm in Fluid Medium

- Velocity Jump Random Walk
  - Motion of motile animals and microorganisms, e.g., Shark’s hunting strategies (*Nature* 2010, 465, 1066-1069)
Simulation Models

- TM swarm moves forward for a time step of random length, governed by a Poisson process with turning frequency $\lambda$

$$f_{\Delta t_i} (\Delta t_i) = \lambda \exp(-\lambda \Delta t_i)$$

- TM swarm changes its direction according to the von Mises distribution, whose mean depends on the propelling field at its present location (directional bias)

$$f_{\Delta \theta_i} (\Delta \theta_i) = \frac{1}{2\pi I_0(\kappa)} \exp(\kappa \cos \Delta \theta_i)$$

- Smaller $\lambda$ corresponds to a more structured fluid network

- Larger $\kappa$ indicates that the propelling force predominates over other microenvironmental gradients
• 9 TM swarms are guided by the propelling field parallel to the horizontal axis. The area is divided into 9 zones with different $\lambda$ and $\kappa$.

• Smaller values of $\lambda$ and $\kappa$ (i.e., larger mean run length and wider spread of turning angles) result in more significant deviation of swarm paths from the preplanned routes.
Propagation of TM Swarm in Vascular Tree
Empirical Models for Blood Vessels

- Generalized Murray’s Law for Vessel Diameters

\[ d_P^\beta = d_{D,1}^\beta + d_{D,2}^\beta \]

β ranges from 2 to 3

- Vessel Length

\[ L = Kd \]

K ≈ 60 for capillaries

- Fractal Dimension

\[ D_F = \frac{\ln 2}{\ln 2 - \ln(1+\lambda^2) + \ln(1+\lambda^\beta)^{2/\beta}}, \text{ where } \lambda = d_{D,2}/d_{D,1} < 1 \]

- Branch angles θ₁ and θ₂

λ is in the range of 0.59 ~ 0.83 for arteries
Random Walk on Vascular Tree

a) Define the injection site on root vessel with diameter $d_{P,0}$ and length $L_{P,0}$. Generate $\beta_0$ and $\lambda_0$ uniformly distributed in $I_\beta$ and $I_\lambda$. Let $i = 1$.

b) At the $i^{th}$ bifurcation, calculate $d_{D,i,1}$, $d_{D,i,2}$, $\theta_{i,1}$ and $\theta_{i,2}$. Generate a random number $Z_i \in \{0,1\}$ that determines the branching direction.

c) At the $i^{th}$ bifurcation, generate $L_{D,i,1}$ and $L_{D,i,2}$ having exponential distribution of means $Kd_{D,i,1}$ and $Kd_{D,i,2}$. Subject to a specific controlling strategy, select the $j^{th}$ ($j = 1,2$) daughter segment to be the traveling path after the $i^{th}$ bifurcation. Define $d_{P,i} = d_{D,i,j}$ and $L_{P,i} = L_{D,i,j}$. Generate $\beta_i$ and $\lambda_i$ uniformly distributed in $I_\beta$ and $I_\lambda$.

d) Check whether the TMs dissolve into the body at the $j^{th}$ branch. If the answer is positive, stop the iteration. Otherwise, go to Step e.

e) Check whether the $j^{th}$ branch intersects the tumor. If the answer is positive, record the arrival position and stop the iteration. Otherwise, increment $i$ by 1 and go to Step b.
Simulated TM Trajectory

- TM path when the boundary of angiographically resolvable vasculature and the diffusion coefficient are set to be $x_r = 6$ cm and $D = 10^{-7}$ m$^2$/s
- The trajectory in $V_r$ has longer and more regular segments
Path Loss

- Diffusion loss increases abruptly as the TM swarm enters $V_{ur}$
- Degeneration loss increases gradually throughout the entire transportation process
• Both pdf of delay and delay spectrum first increase with delay and reach their maximum values, then decrease and exhibit a long tail. Pdfs of delay are concentrated within a broader temporal range.

• Various $D$ do not lead to noticeable changes in pdfs of delay, whereas larger values of $D$ result in smaller delay spreads in delay spectra.
Case Study

a) Assume that a tumor is uniformly distributed within the areas encircled by the 3 dotted ellipses, and concentric magnetic field lines are originated from a dc source via one of the antennas (marked with a “+”). Also shown are the TM survey routes (marked with white curved arrows) covering the surveillance area following the optimized survey plan. The arrow and number indicate the direction and sequence of the TM routes.

b) The TM paths are re-planned (marked with white curved arrows) such that the 8 antennas are sequentially employed to carry a dc for generation of magnetic fields. Assume that the tumor is uniformly distributed within the area encircled by the dotted circle.
**Case Study**

(a) Simulated tumor location (marked with blue circle), which is generated using a spatial uniform distribution within the areas encircled by the 3 dotted ellipses. Also shown are the simulated TM trajectories (marked with thick black curves) following the optimized survey plan.

(b) The probability distributions of the sensing periods for the optimized and non-optimized TM routes.
a) Simulated TM trajectories (marked with thick black curves) following the multidirectional tumor targeting routes. The tumor is marked with red rectangle and the theoretical final footprints are marked with red triangles

b) Simulated final footprints (marked with red squares) for 4 tumors with different sizes
Published Work on this Topic


Summary and Immediate Goals

• Microwave medical imaging
  • Lab prototype by the end of the year to produce images of phantoms
  • Small-scale system for testing with mice using our in-house antennas

• Non-invasive glucose monitoring
  • First clinical trials this summer to test our method
  • Various proposals submitted for next-stage prototype

• New targeted projects
  • Brain Machine Interfaces
  • Hyperthermia and drug delivery methods

• Sensing and Communications at nanoscale
  • Support simulation models with lab work in China
Thank You for your attention!

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