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Abstract

Our contribution is focused on recent research activities in the area of applications of microwaves in medicine and biology. It deals with description of microwave technology in thermotherapy - especially oriented on cancer treatment. Projects on new type hyperthermia applicators (e.g. based on MTM technology, etc.) will be mentioned. Further information about microwaves in medical diagnostics, projects on microwave differential tomography and UWB radar system (both used both for medical diagnostic and for non-invasive temperature measurement as well) will be described. Last but not least, research of biological effects of EM fields (both thermal and non-thermal) will be presented. We will underline international cooperation of Czech researchers with experts from other EU countries.

Keywords Microwave Hyperthermia; Noninvasive Temperature Measurement; UWB Radar; Head and Neck Treatment; Delay and Sum;

1 Introduction

Interactions of EM field with biological systems are utilized in the area of therapy (oncology, physiotherapy, urology, etc.) from late seventieth of last century. Wide utilization of microwave thermotherapy can be observed in the countries of EU, USA, Russia, China, Japan and many others, including the Czech Republic. Important role in development in this area play scientific societies like e.g. ESHO (European Society for Hyperthermia Oncology), which co-operates with STM (Society for Thermal Medicine) and ASHO (Asian Society of Hyperthermia Oncology).

Nowadays the electromagnetic (EM) fields are generally used in several well-established medical applications already. Typical examples are e.g. Computer Tomography (CT) and Magnetic Resonance Imaging (MRI) in medical diagnostics as well as e.g. electro-surgery, radiofrequency (RF) heating in physiotherapy, microwave (MW) hyperthermia and RF + MW ablation in clinical therapy. Therapeutic applications of MWs, e.g. MW hyperthermia and ablation, are being used for the cancer treatment and treatment of some other diseases.

To give a basic overview, we can divide the medical applications of microwaves in following three basic groups according to purpose, how microwaves are used [1-9]:

- Treatment of patients (either thermal or non-thermal effects, sometimes both of these types of effects can play its role).
- Diagnostics of diseases (based on permittivity measurements, very prospective can be a MW differential tomography).
- "Only" a part of a treatment or diagnostic system (like e.g. in case of linear accelerator, etc.).

As is given above, until now medical applications of MW are above all represented by the treatment methods based on thermal effect – i.e. the MW thermotherapy, which can be further divided into three different modalities distinguished according to the goal temperature level or interval:

- Diathermia: heating max up to 41°C (physiotherapy).
- Hyperthermia: heating to interval of 41-45 °C (oncology).
- Thermodestruction/thermoablation: over 45 °C (urology, cardilology fibrillation and arrhytmia treatments).

For here mentioned thermotherapy treatments frequencies from interval from 1 MHz up to 5.6 GHz are mostly used. Recent trends in microwave medical applications are to study the possibilities to develop new diagnostics based on EM field resp. on microwave technique. A significant importance for the future can be identified for the next methods:

- MRI and CT,
- Microwave differential tomography,
- Microwave radiometry,
- Microwave diagnostic radar.

MRI is working mostly in frequency bands from 64 to 299 MHz (upper part of the so called RF band), CT then is working in hard X-ray band. Frequency bands between these two is the MW frequency band, i.e. frequencies from 300 MHz to 300 GHz. Lower part of the MW frequency band, approx. from 300 MHz till 6 GHz, is very prospective for MW medical imaging. Upper part of this frequency band, i.e. frequencies above approx. 100 GHz is very prospective for imaging with Terahertz waves.

We will not mention the MRI and CT technology here, as it is just well known and broadly used application of EM field in medical diagnostics. We will focus here on the other above mentioned methods based on microwave technology.

The use of MWs for medical diagnostics is relatively new but rapidly developing area. The main advantages of MW technology are as follows: MWs belong to a nonionizing radiation and for diagnostics purposes low power levels (1-20 mW) are used only. Furthermore, since the MW technology is being massively used in mobile telecommunication the MW diagnostic systems have potential to be at least one order of magnitude less expensive than MRI.

2 Clinical applications of microwave hyperthermia.

Clinical applications of microwave hyperthermia for cancer treatment started in Prague in the year 1981. It was in cooperation of the Medical Faculty of the Charles University in Prague, the Institute of Radiation Oncology in Prague and the Dept. of EM Field, Faculty of Electrical Engineering, the Czech Technical University in Prague. Microwave hyperthermia has been clinically applied to more than 1000 of cancer patients since that. Mostly added to radiotherapy (RT) and significantly positive contribution to RT treatment has been approved by a clinical study. Recently a combination of hyperthermia added to proton therapy has been clinically applied in Prague.

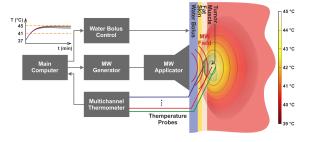


Fig. 1. Schematics of MW hyperthermia system.

In Fig. 1 there is a schematics of the apparatus for the MW hyperthermia treatment. MW power is transmitted to the applicator, which radiates MW power into the area to be treated – and thus creating 3D SAR and 3D temperature distribution according to treatment requirements. Temperature is then measured by invasive sensors and according to it MW power is being controlled in order to keep the temperature on a predetermined level.

3 Technical development.

Technical development of MW thermotherapy and of MW medical diagnostics is in Prague done in cooperation of Dept. of EM Field (Faculty of Electrical Engineering) and Dept. of Biomedical Technique (Faculty of Biomedical Engineering), both belonging to the Czech Technical University in Prague. The most important technical activities in this field can be specified as [2-6]:

- Applicators: development of new applicators for more effective local, intracavitary and regional treatment,
- -Treatment planning: mathematical and experimental modeling of the effective treatment,
- Noninvasive temperature monitoring: e.g. Microwave Differential Tomography or UWB radar technology.
- MW medical diagnostics (e.g. MW Tomography).

We implemented a number of external applicators working at 27, 70, 434 and 2450 MHz. These applicators were used for the treatment of superficial and deep seated tumors (treatment depth from 2 up to 8 cm). Now we continue our research in the direction of new technologies for regional applicators. For that

reason we started to study new microwave technologies, like e.g. metamaterials (MTM), see please the Fig. 2.

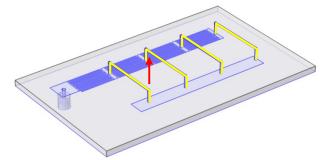


Fig. 2. Aperture view of MTM type applicator. The yellow out–of-plane inductive jumpers (air bridges) connect the interdigital capacitors with parallel referred ground structure. The air bridges have a height of 10 mm above the substrate, which extends 5 mm above the ground plane. Overall dimensions of the structure are $190 \times 120 \times 15.1 \text{ mm}^3$. The red arrow shows the direction of propagation into tissue.

Here described MTM applicators are being developed in a cooperation of the Dept. of Biomedical Technique with Prof. Paul Stauffer from Thomas Jefferson University Hospital in Philadelphia.

In Fig. 3 there is an example of the temperature distribution obtained by a matrix of $3x^2$ aperture array. Highest level of the temperature is displayed here in red color, yellow color denotes the threshold therapeutic temperature of 41° C.

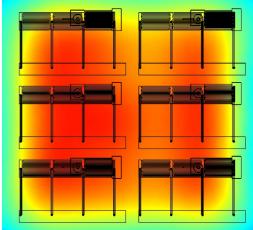


Fig. 3. Temperature distribution at 3.5 cm depth under the 3×2 aperture array. The yellow color denotes the threshold therapeutic for

For the treatment planning we need to create phantoms of the patient body or at least of the area to be treated, see please Fig. 4a,b. In the Fig. 4a there is an example of a homogeneous phantom, in Fig. 4b then there is example of the anatomical phantom. Homogeneous phantom is good for verifying of the basic behavior of the applicator, Anatomical phantom then is needed for the 3D SAR and 3D temperature distribution during the treatment of the real patient.

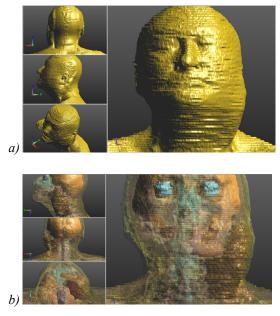


Fig. 4. Example of a homogeneous (a) and the anatomical phantom (b).

In Fig. 5 then there is given an example of a SAR distribution calculated for the case of anatomical phantom given in Fig. 5. A very nice focusing of MW power into a big tumor can be observed here.

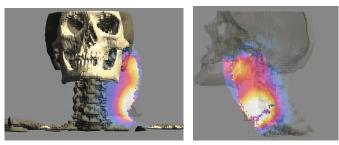
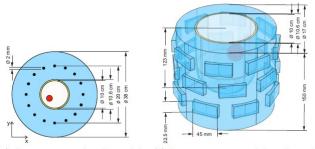


Fig. 5. Example of SAR distribution calculated for the case of anatomical phantom given in Fig. 4.

4 Microwave medical diagnostics

B. Microwave differential tomography (MDT)

MDT is in Prague developed by people from Dept. of Biomedical Technology in cooperation with Prof. Andrea Massa and his group from ELEDIA Research Center (University of Trento, Italy). Theoretical works are focused on a theory of a Differential Microwave Imaging (DMI) in quasi real time. Existing suitable reconstruction algorithms, namely Distorted Born Algorithm (DBA) and Born Algorithm (BA), which allow quasi-real-time monitoring of changes of dielectric properties due to change of temperature, were implemented. They were applied and tested both numerically and experimentally within the feasibility studies. Reconstruction algorithms were firstly tested on numerical data from different numerical 2D and 3D simulations, see numerical models in the Fig. 6.



(a) Cross-section of a 2D model (b) Perspective view of the 3D model

Fig. 6. Numerical models for testing of reconstructions algorithms.

The obtained results using DBA and BA were compared in terms of algorithms ability to reconstruct shape and position of the target and flatness of the obtained object function in regions without change in dielectric properties. Furthermore, influences of different TSVD-threshold values, number of pixels and normalization were tested. BA with low TSVDthreshold value leads to clear pictures of difference in relative permittivity, but we lose information about difference in conductivity. Described algorithms were tested with sphere virtually homogeneously heated and resulting pictures have no clear boundary of the object function: the predicted changes of object function are smooth, see please Fig. 7 and 8. Even though the implemented algorithms show several deficits they represents state-of-the-art and are therefore suitable starting point in development of the combined system. Such noninvasive temperature monitoring, when it will be available, would mean a significant improvement of Quality Assurance for hyperthermia treatment of oncological patients in real clinics. And for the comfort of their treatment as well.

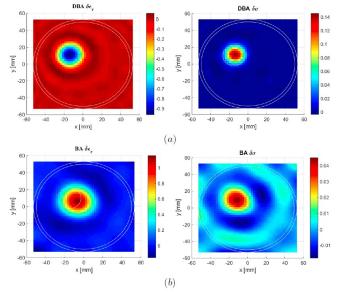


Fig. 7. Results of reconstruction on 2D model.

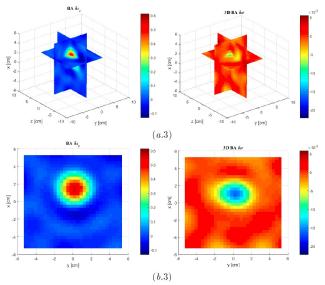


Fig. 8. Results of reconstruction on 3D model.

In Fig. 9 there is a photograph of laboratory MDT system, which was built at the Dept. of Biomedical Technique. The system currently consists of 8 bow-tie antennas. All necessary MATLAB scripts for measurements automatization, data acquisition and image reconstruction were implemented. Numerical models for solving the forward problem necessary for the reconstruction algorithms were created. At the same time preliminary evaluation of the system based on measurement results was performed.

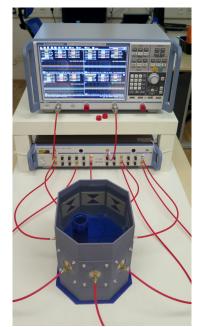


Fig. 9. Photograph of an experimental system for research of MDT.

It seems to be realistic that the DMI methods can be used for 3D non-invasive temperature monitoring of the treated volume during thermotherapy in oncology.

In near future it is planned to analyze the suitability of various types of antennas, their size, number and different placements by means of numerical simulations. Furthermore, we believe, that the main resolution limit of the current here described system is a low number of antennas. We plan to extend the system to the maximum possible number of antenna elements of our current measurement equipment (i.e. up to 24) and therefore there is considerable potential for improvement.

Other prospective possibility to use DMI is the very quick detection, identification and classification of strokes (SDI), which would be very essential for quick qualified decision of what kind of treatment is necessary to give to the stroke patient already in ambulance, when he/she is being transferred to the hospital. Pioneer research group in this area is a team of Prof. Mikael Persson from Chalmers University in Goeteborg, Sweden

C. UWB radar

Microwave UWB radar technology for noninvasive microwave imaging and/or noninvasive temperature monitoring is in Prague developed by people from Dept. of EM Field in cooperation with Dr. Marko Helbig and Dr. Juergen Sachs from TU Ilmenau in Germany [8, 9].

References

1. Vrba, J et al.: "Technical Aspects of Microwave Thermotherapy". RF Interaction with Humans: Mechanisms, Exposures and Medical Applications. IPEM Meeting, Inst. of Physics, London, February 2003

2. Vrba, J., Franconi, C. Montecchia, F., Vanucci, I.: "Evanescent Mode Applicators for Subcutaneous Hyperthermia". IEEE Trans. on Biomedical Engineering, Vol.40, No 5, May 1993, pp. 397 – 407

3. Franconi, C., Vrba, J., Montecchia, F.: "27 MHz Hybrid Evanescent-Mode Applicators with Flexible Heating Field for Deep Hyperthermia". Int. Journal of Hyperthermia, 1993, Vol. 9., No. 5., pp. 655 – 673

4. H.Trefna, J.Vrba, M.Persson, "Time-reversal focusing in microwave hyperthermia for deep-seated tumors," Physics in Medicine and Biol., vol. 55, no. 8, pp. 2167–2185, Apr. 2010.

5. D. Vrba, J. Vrba, "Novel Applicators for Local Microwave Hyperthermia Based on Zeroth-Order Mode Resonator Metamaterial," *International Journal of Antennas and Propagation*, vol. 2014, pp. 1-7, 2014.

6. D. Vrba, J. Vrba, D. B. Rodrigues, P. Stauffer: "Numerical Invest. of Novel Microwave Applicators Based on Zero-Order Mode Resonance for Hyperthermia Treatment of Cancer".

7. Vrba, J., Oppl, L., Vrba_{jr}, J., Vrba, D.: Microwave Medical Imaging and Diagnostics. In EuMW 2008, Conference Proceedings. London: Horizon House Publications, 2008, p. 408-411. ISBN 978-1-4244-3794-8.

 O. Fiser, M. Helbig, S. Ley, J. Sachs, and J. Vrba, "Feasibility study of temperature change detection in phantom using M-sequence radar," in 2016 10th EuCAP, 2016, pp. 1–4.
O. Fiser, I. Merunka, J. Vrba: "Numerical Feasibility Study of New Combined Hyperthermia System for Head and Neck Region", th European Microwave Conference (EuMC), 2017