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Improving the accuracy of tumor surgery by THz imaging and making the results of pathological anatomy faster by THz spectroscopy

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Abstract

Background: The terahertz radiation is a specific part of the electromagnetic radiation spectrum and has multiple significant applications in multiple scientific researches such as the applications in the medicine. An important application of the terahertz is its use in tumor imaging which is very important in the tumor surgery; however, lots of physicians and workers in the medical field have little information or having no information at all, dealing with this significant part of the electromagnetic spectrum.

Results: In this work, we interviewed a number of local surgeons in Syrian Arab Republic, who reported that they visually delineate the contour of tumors to be removed, and in order to reduce the number of future possible interventions, a large margin of healthy tissue is often excised. Furthermore, a number of pathologists who reported that preparing samples of excised tissues for examination takes a long period of time which may extend to several days, and that the results of histopathology indicate in some cases the integrity of removed tissues.

Conclusion: We have found that a significant number of participants in the survey demonstrated that the importance of dealing with terahertz imaging and terahertz spectroscopy, encouraging to implement the technique in the Syrian Arab Republic.

Keywords: Terahertz radiation, Surgery, THz imaging, THz spectroscopy, Far-infrared radiation

1 Background

Terahertz frequency (THzF) radiation lies between two safe (Fig. 1), non-ionizing regions of the electromagnetic spectrum: the microwave and the infrared. It can be generated by up-conversion from sources of micro-waves, or by down-conversion from sources of higher frequency [56]. It is strongly absorbed by polar molecules like water, that is why it is very sensitive to any difference in water content between healthy tissue and a tumor [49, 59]. Due to the non-ionizing nature of THz light and its high

sensitivity to soft tissues, there is an increasing interest in biomedical applications including both in vivo and ex vivo studies.

Thanks to the development of terahertz sources and detectors of continuous and pulsed wave, methods of terahertz imaging (THzI) (CWI or TPI in reflection geometry) in vivo and ex vivo have spread rapidly [17–19, 21, 47–49, 51–54].

Investigations about various tissues to discriminate between healthy and malignant breast tissues were carried out [1, 2, 5, 6, 8, 13, 18, 25, 36, 40, 47, 51–54, 56].

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Fig. 1 The spectrum of the terahertz radiation

Okada et al. [32] who reported terahertz near-field microscopy of ductal carcinoma in situ (DCIS) of the breast, Vafapour et al. [42] who reported the potential of terahertz sensing for cancer diagnosis, Ke et al. [26, 27] used THz technology in vivo sensing of rabbit cornea, Cassar et al. [7] who reported investigations led on the combination of the refractive index and morphological dilation to enhance performances toward breast tumor margin delineation during conserving surgeries. Smolyanskaya et al. [35] discussed in their review THz dielectric permittivity of water and water-containing media, using THz time-domain spectroscopy and spectroscopy, and sub-wavelength resolution THz imaging.

1.1 Image data treatment

A number of algorithms some with numerical simulation [3] were developed to process THz image data [33]. Studies about pattern identification in a series of medical images recorded in a timestamps were carried out [57]; approaches for image-huge data supervised classification using support vector machine (SVM) [20] and unsupervised clustering using k-means [one of machine learning algorithms] [4] were developed. Ornstein–Uhlenbeck process used to distinguish Malignant and benign thyroid nodule [16, 22, 24, 28–30, 41].

1.2 THz radiation effects

Various studies about THz effects on biological tissues were carried out [50]. Sun et al. [38] reported that THz light is absorbed by H-bonds presents in water and proteins, deducing its sensitivity to any change in water or blood content. Son et al. [36] reported in their review that methylated malignant DNA exhibits a characteristic resonance at approximately 1.65 THz, which may help in treating cancer through the demethylation of malignant DNA using high-power terahertz pulse at this specific frequency. Cherkasovaa et al. [9] discussed in their review THz thermal effects on tissue and its ability to induce resonance effects. With high energy pulse, THz radiation may penetrate the cytoplasm and the membrane of the nucleus. Nikitkina et al. [31] reported in their review the effects of THz radiation and problems of using it in medical diagnosis, THz Dosimetry, effects of this Radiation on Blood, Skin, Nerve and Stem Cells, and mechanism that underlie the effects of THz Radiation and showed the possibility of cancer therapy using the appropriate intensity of THz waves, depending the case [10–12, 14, 15, 37, 39, 43–58].

1.3 The aim of the work

The aim of this work was measuring the awareness of medical community in our country in order to apply the THz technology to improve the resolution of tumor surgery and may be, treating certain cases of cancer. The availability of THz imaging and spectroscopic techniques and their ability to distinguish between benign and malignant tissues, as well as the possibility to heal some tumors by THz exposure encourage us to set off our project.

2 Methods

The latter facts motivated us to launch, using Google forms, a survey of 33 questions to obtain information about the scientific community's awareness of the use of THz technique in Syrian Arab Republic, with an ambition to make tumor surgery more accurate and results of histopathology of excised tissues faster. The survey consisted of 2 groups of questions. The first group, which aims to promote practicing THz methods in Syrian Arab Republic, involves 28 questions concerning THz waves, sources, properties, uses in tissue imaging and spectroscopy, and its importance in pain relieving for patients who bore a tumor surgery. The second group of 5 questions concerns the knowledge of some information about

THz Technique. The survey targeted scientific faculties: Medicine, Dentistry, Pharmacy, Science and other faculties, of various qualifications ranging from undergraduates to university degree, M.A degree and Ph.D. We used IBM SPSS statistics 26 software (Lawrence 1983, [34], and [23] for analyzing the results.

The survey was launched on google drive, and the data were transferred to an excel file, where problems regarding survey were resolved and then, was translated into English. From the order of filtering order, we obtained the distribution of survey participants by qualification and distribution of survey participants by specialty.

We set up a page of data view and variable view on SPSS statistic program, version 26, that is filled, for each specialty by the numbers of participants from all qualifications and for each qualification by the numbers of participants from all specialties. From Graphs-Legacy Dialogs-line -Simple-Summaries for groups of cases, we obtained the first group of curves. Figure 2 represents distribution of survey participants by qualification. Figure 3 represents distribution of survey participants by specialty. Figures 4, 5, 6, 7 and Additional file 1: Fig. S1 show distribution of each specialty participants by qualification; Figs. 8, 9, 10 and 11 show distribution of each qualification participants by specialty.

Fig. 3 Distribution of survey participants by specialty

Fig. 4 Distribution of survey dentistry participants by qualification

Fig. 5 Distribution of survey medicine participants by qualification

Fig. 6 Distribution of survey pharmacy participants by qualification

Fig. 7 Distribution of survey science participants by qualification

Fig. 8 Distribution of survey other participants by qualification

Fig. 9 Distribution of survey college degree participants by specialty

Fig. 10 Distribution of survey college student participants by specialty

To get the rest of the curves, we followed these steps: from file-import data-excel, we transferred the survey file from an excel file to the statistical program SPSS.

The curves of the first group of survey questions in Figs. 12a, b, 13a, b, 14a, b, 15a, b and Additional file 1: Fig. S2 were prepared for, by splitting data file by qualification, whereas curves in Figs. 16a, b, 17a, b, 18a, b, 19a,

Fig. 11 Distribution of survey M.A degree participants by specialty

Fig. 12 **a** I know it from cultures and **b** I don't know

b were prepared for, by splitting data file by specialties. Figures (a) for the choice: I know it from cultures, (b) for the choice: I don't know. A table is made for each group of curves.

Curves of Figs. 20a–d, 21a–d, 22a–d, 23a–d and Additional file 1: Fig. S3 were prepared for by splitting data file by qualification, and curves Figs. 24a–d, 25a–d, 26a–d

and 27a–d by splitting data file by specialty. A table was set for each group of curves. (a) for the choice: Yes, (b) for: No, (c) for: May be, and (d) for: I don't know.

Each group of curves in a figure is obtained as follows: Graphs-Legacy Dialogs-line -Multiple-Summaries for Separate Variables.

3 Results

When interviewed, a number of local oncologists in the Syrian Arab Republic who reported that they visually delineate the contour of the tumor to be removed, and in order to reduce the number of future possible interventions, a large margin of healthy tissue is often excised (This precaution, however, reflects negatively on the speed of healing process). Furthermore, a number of pathologists who reported that preparing samples of excised tissues for examination takes a long period of time which may extend to several days, and that the

results of histopathology indicate in some cases the integrity of removed tissues. Studies taking place currently in some parts of the world show that, owing to the THz sensitivity to tissue content of water, which increases in case of tumors, THz imaging can delineate tumor contour with a high precision. At present, studies of excised tissues are carried out utilizing each of the metabolites signature in a tissue when subjected to the terahertz radiation, as well as, the capability of this radiation to distinguish malignant tumor from benign ones without need to a preparation process.

The number of participants in the survey was 1549 after deleting the wrong cases. Figure 2 illustrates the distribution of survey participants by Qualification, while Fig. 3 shows the distribution of survey participants by Specialty. The participation of College Students (Fig. 2) from different specialties was the highest (696, 44.9%, and in particular, participants with a background in medicine (Fig. 3) of various qualifications (college degree, college student, M.A and Ph.D.) were highest (873, 56.36%). Figures 4, 5, 6 and 7 show the statistical distributions of the

survey participants from Dentistry, Medicine, Pharmacy and Science (Other faculties) according to Qualification, and that the participation of the college students is the highest regardless of their specialty. Figures 8, 9, 10 and 11 show the statistical distributions for the qualification levels, college degree, college student, M.A and Ph.D., respectively, with their specialty is the variable. Regardless of their qualification's level, medical participants were always dominant.

The answer choices for the second group of survey questions were

1. Yes.
2. No.
3. May be.
4. I don't know.

4 Discussion

4.1 Statistical results of the first group of questions

The answers were distributed, in particular, between the third choice and the last one. To deduce the information describing the awareness of the Scientific Community of THz technique, we plotted the statistic curves for those who chose “I know it from lectures” and for those who

selected “I don’t know” for all the participants of various specialties and qualifications and for all the questions. The ratios of other answer choices (1, 2, 4 and 5) were very low. The curves showed a magnificent coherence between various qualifications in a specialty (Figs. 12, 13, 14, 15) with a minor exception. The curves of Additional file 1: Fig. S2a show very little coherence between various qualifications in other specialties (Medical Engineering, Informatics, ...), while Additional file 1: Fig. S2b show a slightly higher degree of coherence. Figures 16, 17, 18 and 19 show the strong degree of coherence between

various specialties in a qualification. The total number of participants in the survey with medicine background reached 873, of which 402 (46.0%), are undergraduates, 297 (34.0%) with a university degree, 117 (13.4%) with a master’s degree, and 57 (6.5%) are Ph.D. holders (Fig. 12a, b).

For the dentistry, the total number of participants in the survey with dentistry background is 228, of which 105 (46.1%) are undergraduates, 64 (28.1%) with a university degree, 47 (20.6%) with a master degree, and 12 (5.3%) are Ph.D. holders (Fig. 13a, b). For the Pharmacy, the

total number of participants in the survey with pharmacy background reached 124 members, of which 52 (41.9%) are undergraduates, 45 (36.3%) with university degree, 24 (19.4%) with a M.A. degree, and 3 (2.4%) Ph.D. holders, Fig. 14a, b, while for the science, the total number of participants in the survey with Science background is 244 members, of which 110 (45.1%) are undergraduates, 87 (35.7%) with a University degree, 24 (9.8%) with a M.A. and 23 (9.4%) are Ph.D. holders (Fig. 15a, b).

Finally for the Other Specialties (Medical Engineering, Informatics, ...), the total number of participants

in the survey with various specialties background is 80 members, of which 27 (33.8%) are undergraduates of various specialties, 28 (35.7%) with a University degree, 19 (23.8%) with a master's degree and 6 (7.5%) are Ph.D. holders (Additional file 1: Fig. Fig. S2a, b).

By classifying the answers based on undergraduate students, the total number of participants is 696, 402 (57.76%) of medicine, 105 (15.09) of dentistry, 52 (7.47%) of pharmacy, 110 (15.80%) of science and 27(3.88%) of other faculties, Fig. 16a, b. For university degree of various specialties, the total number of participants is 521,

of which 297 (57.01%) of medicine, 64 (12.28%) of dentistry, 45 (8.64%) of pharmacy, 87 (16.70%) of science and 28(5.37%) of other faculties (Fig. 17a, b). For Master's degree holders in any specialty, the total number of participants is 231, of which 117 (50.65%) in medicine, 47 (20.35%) in dentistry, 24 (10.39%) in pharmacy, 24 (10.39%) in science and 19(8.23%) in other faculties (Fig. 18a, b). For the Ph.D. holders in any specialty, the total number of participants is 101, of which 57 (56.44%) in medicine, 12 (11.88%) in dentistry, 3 (2.9%) in pharmacy, 23 (22.77%) in science and 6 (5.94%) in other faculties (Fig. 19a, b).

4.2 Statistical results of the second group of survey questions

The answers were distributed between the 4 choices. We plotted the statistic curves for each choice for all the participants of various specialties and qualifications and for all the 5 questions. The curves show highly coherent response of participants of various qualifications in each specialty (Figs. 20, 21, 22, 23), with some exception. The curves of Additional file 1: Fig. S3a–d show much less coherence, for some choices, between various qualifications from faculties that are less concerned with the

technique of terahertz. Figures 24, 25, 26 and 27 show the coherence between various specialties in a qualification. For the medicine of various qualifications, Fig. 20a–d, for the choices 1, 2, 3 and 4, respectively.

For the dentistry of various qualifications, Fig. 21a–d, for the choices 1, 2, 3 and 4, respectively. For the pharmacy of various qualifications, Fig. 22a–d, for the choices 1, 2, 3 and 4, respectively, and for the science of various qualifications, Fig. 23a–d, for the choices 1, 2, 3 and 4, respectively, while for the Other specialties (Medical

Engineering, Informatics, ...) of various qualifications, Additional file 1: Fig. S3a–d, for the choices 1, 2, 3 and 4, respectively.

For the Undergraduate students of various specialties, Fig. 24a–d, for the choices 1, 2, 3 and 4, respectively. For the university degree of various specialties, Fig. 25a–d, for the choices 1, 2, 3 and 4, respectively. For M.A., of various specialties, Fig. 26a–d, for the choices 1, 2, 3 and 4, respectively, and for Ph.D. of various specialties, Fig. 27a–d, for the choices 1, 2, 3 and 4, respectively.

5 Conclusions

This result is logic. The first author was engaged in teaching medical physics for students of medicine at Damascus University since 3 decades. 8 years ago engaged in teaching Medical Physics to students of dentistry at Syrian Private University, meanwhile engaged in the program of Physics for Preparatory year for medical colleges (medicine, dentistry and pharmacy). That is why most of the survey participants were undergraduate students of medicine, fewer young physicians of different specialties, comprising radiologists, M.A and PHd.

From the above curves, we have found that the great coherence of awareness between participants of various qualification with medicine and dentistry background, less coherence with faculties that are less concerned with the technique of Terahertz. A significant number of participants in the survey provided us, on messenger, with comments demonstrated that the importance of dealing with THz imaging and THz spectroscopy, encouraging to implement the technique in the Syrian Arab Republic. We present in this paper some comments for undergraduate students of medicine, physicians and pharmacists.

Fig. 26 a I don't know, b may be, c yes and d no

A significant number of participants in the survey provided us (on messenger) with comments that highlight the importance of adopting THz imaging and THz spectroscopy and urge encourage to implement this

technique in the Syrian Arab Republic. We present in this paper some comments for undergraduate students of medicine, physicians and pharmacists.

Abbreviations

THz: Terahertz radiation; College. Stu. Med. N: College students of Medicine Number; College. deg. Med. N: College degree of Medicine Number; College. Stu. Den. N: College student of dentistry Number; College. deg. Den. N: College degree of dentistry Number; College. Stu. Pha. N: College student of pharmacy Number; College. deg. Pha. N: College degree of pharmacy Number; College. Stu. Sci. N: College student of science Number; College. deg. Sci. N: College degree of science Number; College. Stu. Oth. N: College students of other faculties Number; College. deg. Oth. N: College degree of other faculties Number.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s43088-022-00201-7>.

Additional file 1: Distributions of Other participants by qualifications.

Acknowledgements

We would like to thank Amjad Hijazi, Head of Networks Section, Operating Systems and IT support at SPU; Abdulhadi Awad, IT support at SPU and Marah Marrawi, Statistical Unit at SPU, for their help during carrying on statistical study of the survey data.

Authors' contributions

All authors of the article: ST; MA and OS are responsible to the design and implementation of the research to the analysis of the results and to the writing of the manuscript. All authors read and approved the final manuscript.

Funding

Not applicable.

Availability of data and materials

The author confirms that the data available for non-commercial using.

Declarations

Ethics approval and consent to participate

The Syrian Private University granted the study a waiver with number 04072020. All the participants in the study agreed to participate in the survey.

Consent for publication

Not applicable.

Competing interests

The authors have no conflict of interests to declare.

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Received: 19 August 2021 Accepted: 20 January 2022

Published online: 14 February 2022

References

- Ahi K, Jessurun N, Hosseini M, Asadizanjani N (2020) Survey of terahertz photonics and biophotonics. *Opt Eng* 59(6):061629. <https://doi.org/10.1117/1.OE.59.6.061629>
- Alkhayrat M, Aljndi M, Aljoumaa K (2020) A comparative dimensionality reduction study in telecom customer segmentation using deep learning and PC. *J Big Data* 7(1):9. <https://doi.org/10.1186/s40537-020-0286-0>
- Al-Raei M (2021) Applying fractional quantum mechanics to systems with electrical screening effects. *Chaos Solitons Fractals* 150(C):111209. <https://doi.org/10.1016/j.chaos.2021.111209>
- Ayech MW, Ziou D (2015) Segmentation of terahertz imaging using k-means clustering based on ranked set sampling. *Expert Syst Appl* 42(6):2959–2974. <https://doi.org/10.1016/j.eswa.2014.11.050>
- Al-Ibadi A, Sleiman JB, Cassar Q, MacGrogan G, Balacey H, Zimmer T, Mounaix P, Guillet JP (2017) Terahertz biomedical imaging: from multivariate analysis and detection to material parameter extraction. Paper presented at the Progress in electromagnetics research symposium, pp 2756–2762. <https://doi.org/10.1109/PIERS.2017.8262222>
- Bowman T, Wu Y, Gauch J, Campbell LK, El-Shenawee M (2017) Terahertz imaging of three-dimensional dehydrated breast cancer tumors. *J Infrared Millim Terahertz Waves* 38(6):766–786. <https://doi.org/10.1007/s10762-017-0377-y>
- Cassar Q, Caravera S, MacGrogan G, Bücher T, Hillger P, Pfeiffer U, Zimmer T, Guillet JP, Mounaix P (2021) Terahertz refractive index-based morphological dilation for breast carcinoma delineation. *Sci Rep* 11(1):1–16. <https://doi.org/10.1038/s41598-021-85853-8>
- Cacciari I, Ciofini D, Bajja H, Siano S (2019) Terahertz time-domain reconstruction of coating microstratigraphy on gilded surfaces. *Materials* 12(23):3822. <https://doi.org/10.3390/ma12233822>
- Cherkasova OP, Serdyukov DS, Ratushnyak AS, Nemova EF, Kozlov EN, Shidlovskii YV, Zaytsev KI, Tuchin VV (2020) Effects of terahertz radiation on living cells: a review. *Opt Spectrosc* 128(6):855–866. <https://doi.org/10.1134/S0030400X20060041>
- Cherkasova O, Peng Y, Konnikova M, Kistenev Y, Shi C, Vrazhnev D, Shevelev O, Zavjalov E, Kuznetsov S, Shkurinov A (2021) Diagnosis of glioma molecular markers by terahertz technologies. *Photonics* 8(1):1–30. <https://doi.org/10.3390/photonics8010022>
- Chizhov PA, Ushakov AA, Bukin VV, Garnov SV (2019) Terahertz radiation from extended two-colour air filaments. *Laser Phys Lett* 16(7):075301. <https://doi.org/10.1088/1612-202X/ab2054>
- Chulkov R, Goryashko V, Arslanov DD, Jongma RT, Van Der Zande WJ, Zhaunerchyk V (2014) Multimode dynamics in a short-pulse THz free electron laser. *Phys Rev Spec Top Accel Beams* 17(5):050703. <https://doi.org/10.1103/PhysRevSTAB.17.050703>
- Danciu M, Alexa-Stratulat T, Stefanescu C, Dodi G, Tamba BI, Mihai CT, Stanciu GD, Luca A, Spiridon IA, Ungureanu LB, Ianole V (2019) Terahertz spectroscopy and imaging: a cutting-edge method for diagnosing digestive cancers. *Materials (Basel)* 12(9):1519. <https://doi.org/10.3390/ma12091519>
- Dong J, Breitenborn H, Caraffini D, Piccoli R, Govorov AO, Razzari L, Naccache R, Vetrone F, Morandotti R (2019) Investigation of nanoparticle-assisted laser tissue soldering by terahertz radiation. Paper presented at the Optics InfoBase conference papers, part F140-CLEO_Europe 2019
- Dong J, Breitenborn H, Piccoli R, Besteiro LV, You P, Caraffini D, Wang ZM, Govorov AO, Naccache R, Vetrone F, Razzari L (2020) Terahertz three-dimensional monitoring of nanoparticle-assisted laser tissue soldering. *Biomed Opt Express* 11(4):2254–2267. <https://doi.org/10.1364/BOE.389561>
- Elayan H, Shubair RM, Almoosa N (2017) In vivo communication in wireless body area networks. In: *Information innovation technology in smart cities*, pp 273–287. https://doi.org/10.1007/978-981-10-1741-4_18
- Fitzgerald AJ, Berry E, Zinovev NN, Walker GC, Smith MA, Chamberlain JM (2002) An introduction to medical imaging with coherent terahertz frequency radiation. *Phys Med Biol* 47(7):R67–R84. <https://doi.org/10.1088/0031-9155/47/7/201>
- Fitzgerald AJ, Wallace VP, Jimenez-Linan M, Bobrow L, Pye RJ, Purushotham AD, Arnone DD (2006) Terahertz pulsed imaging of human breast tumors. *Radiology* 239(2):533–540. <https://doi.org/10.1148/radiol.239204315>
- Geetharamani G, Aathmanesan T (2019) Metamaterial inspired THz antenna for breast cancer detection. *SN Appl Sci* 1(6):1–9. <https://doi.org/10.1007/s42452-019-0601-6>
- Grootendorst MR, Fitzgerald AJ, De Koning SG, Santaolalla A, Portieri A, Van Hemelrijck M, Young MR, Owen J, Cariati M, Pepper M, Wallace VP (2017) Use of a handheld terahertz pulsed imaging device to differentiate benign and malignant breast tissue. *Biomed Opt Express* 8(6):2932–2945. <https://doi.org/10.1364/BOE.8.002932>
- He M, Chen T, Yang J, Liu J (2012) The application of terahertz imaging in tumor diagnosis. *Tumor* 32(12):1039–1042. <https://doi.org/10.3781/jissn.1000-7431.2012.12.016>
- Hintzsche H, Jastrow C, Heinen B, Baaske K, Kleine-Ostmann T, Schwedtfeger M, Shakfa MK, Käst U, Koch M, Schrader T, Stopper H (2013) Terahertz radiation at 0.380 THz and 2.520 THz does not lead to DNA damage in skin cells in vitro. *Radiat Res* 179(1):38–45. <https://doi.org/10.1667/RR3077.1>
- Ibrahim UM, Umar ML, Gajida AU, Jalo RI, Onimisi OS, Zubairu Z, Okakah F, Nasidi KN (2020) Health risks associated with consumption of fast foods: perspectives of traders in Kano, Nigeria Niger. *J Nutr Sci* 41(2):35–45
- Jung E, Park H, Kim J, Han Y, Han H, Kim S, Park I, Cui J, Min B, Lim H (2006) Terahertz pulse imaging of human articular cartilage. Paper presented at the IRMMW-THz 2006—31st International conference on infrared and millimeter waves and 14th international conference on terahertz electronics, p 550. <https://doi.org/10.1109/ICIMW.2006.368758>
- Kan W, Lee W, Cheung W, Wallace VP, Pickwell-MacPherson E (2010) Terahertz pulsed imaging of knee cartilage. *Biomed Opt Express* 1(3):967–974. <https://doi.org/10.1364/BOE.1.000967>
- Ke L, Zhang N, Qing Yang Steve W, Sergey G, Abdelaziem A, Liu Z, Erica Pei Wen T, Mehta JS, Liu YC (2021) In vivo sensing of rabbit cornea by terahertz technology. *J Biophotonics*. <https://doi.org/10.1002/jbio.20210130>
- Ke L, Wu QYS, Zhang N, Yang Z, Teo EPW, Mehta JS, Liu Y (2021) Terahertz spectroscopy analysis of human corneal sublayers. *J Biomed Opt* 26(4):043011. <https://doi.org/10.1117/1.JBO.26.4.043011>
- Llatser I, Kremers C, Chigrin DN, Jornet JM, Lemme MC, Cabellos-Aparicio A, Alarcón E (2012) Characterization of graphene-based nano-antennas in the terahertz band. Paper presented at the Proceedings of 6th European Conference on Antennas and Propagation, EuCAP 2012, pp 194–198. <https://doi.org/10.1109/EuCAP.2012.6206598>
- Jin-Long M, Kai-Jun X, Zhe L, Biao-Bing J, Rong F, Cai-Hong Z, Zheng-Ming J, Cang Z, Zhao-Xu C, Jian C, Pei-Heng W (2009) Temperature-dependent terahertz spectroscopy of D-, L- and DL-ornidazole. *Wuli Xuebao/Acta Phys Sin* 58(9):6101–6107
- Mallik S, Singh PK, Ahmad G, Guhathakurata S, Mahato SS, Manik NB (2021) High-sensitive terahertz biosensors. https://doi.org/10.1007/978-981-33-4489-1_17
- Nikitkina AI, Bikmulina PY, Gafarova ER, Kosheleva NV, Efremov YM, Bezrukov EA, Butnaru DV, Dolganova IN, Chernomyrdin NV, Cherkasova OP, Gavdush AA (2021) Terahertz radiation and the skin: a review. *J Biomed Opt* 26(4):043005. <https://doi.org/10.1117/1.JBO.26.4.043005>
- Okada K, Serita K, Cassar Q, Murakami H, MacGrogan G, Guillet JP, Mounaix P, Tonouchi M (2020) Terahertz near-field microscopy of ductal carcinoma in situ (DCIS) of the breast. *J Phys Photonics* 2(4):044008. <https://doi.org/10.1088/2515-7647/abbcda>
- Parrott EP, Sy SM, Blu T, Wallace VP, Pickwell-MacPherson E (2011) Terahertz pulsed imaging in vivo: measurements and processing methods. *J Biomed Opt* 16(10):106010. <https://doi.org/10.1117/1.3642002>
- Por CS, Keshavarzi F, Yap CS, Soh YC (2020) Knowledge, attitude and practice of general public towards counterfeit and adulterated medicines: a cross-sectional study in Malaysia. *Curr Trends Biotechnol Pharm* 14(5):82–91. <https://doi.org/10.5530/ctbp.2020.4s.9>
- Smolyanskaya OA, Chernomyrdin NV, Konovko AA, Zaytsev KI, Ozheredov IA, Cherkasova OP, Nazarov MM, Guillet JP, Kozlov SA, Kistenev YV, Coutaz

- JL (2019) Terahertz biophotonics as a tool for studies of dielectric and spectral properties of biological tissues and liquids. *Prog Quantum Electron* 62:1–77. <https://doi.org/10.1016/j.pquantelec.2018.10.001>
36. Son J, Oh SJ, Cheon H (2019) Potential clinical applications of terahertz radiation. *J Appl Phys* 125(19):190901. <https://doi.org/10.1063/1.5080205>
 37. Stoyanov NS, Ward DW, Feurer T, Nelson KA (2002) Terahertz polariton propagation in patterned materials. *Nat Mater* 1(2):95–98. <https://doi.org/10.1038/nmat725>
 38. Sun Q, He Y, Liu K, Fan S, Parrott E, Pickwell-Macpherson E (2017) Recent advances in terahertz technology for biomedical applications. *Quant Imaging Med Surg* 7(3):345–355. <https://doi.org/10.21037/qims.2017.06.02>
 39. Sudworth CD, Fitzgerald AJ, Berry E, Zinov'ev NN, Homer-Vanniasinkam S, Miles RE, Chamberlain M, Smith MA (2003) The optical properties of human tissue at terahertz frequencies. Paper presented at the Proceedings of SPIE—the international society for optical engineering, pp 5143_59–68
 40. Tarabichi S, Achkar B, Sayem El-Daher M (2016) Physics for the preparatory year of medical colleges. Ministry of Higher Education Publishing, the Syrian Arab Republic
 41. Taylor ZD, Singh RS, Culjat MO, Suen JY, Grundfest WS, Brown ER (2008) THz imaging based on water-concentration contrast. Paper presented at the Proceedings of SPIE—the international society for optical engineering, vol 6949. <https://doi.org/10.1117/12.785337>
 42. Vafapour Z, Keshavarz A, Ghahraloud H (2020) The potential of terahertz sensing for cancer diagnosis. *Heliyon* 6(12):e05623. <https://doi.org/10.1016/j.heliyon.2020.e05623>
 43. Vainshtein SN, Duan G, Yuferev VS, Zemlyakov VE, Egorkin VI, Kalyuzhnyy NA, Maleev NA, Egorov AY, Kostamovaara JT (2019) Collapsing-field-domain-based 200 GHz solid-state source. *Appl Phys Lett* 115(12):123501. <https://doi.org/10.1063/1.5091616>
 44. Vohra N, El-Shenawee M, Bailey K (2020) Dehydration approach for enhancing terahertz detection of cancer in freshly excised breast tumors. Paper presented at the 2020 IEEE international symposium on antennas and propagation and North American radio science meeting, IEEECONF 2020—Proceedings, pp 43–44. <https://doi.org/10.1109/IEEECONF35879.2020.9330034>
 45. Wallace VP, Fitzgerald AJ, Shankar S, Flanagan N, Pye R, Cluff J, Arnone DD (2004) Terahertz pulsed imaging of basal cell carcinoma ex vivo and in vivo. *Br J Dermatol* 151(2):424–432. <https://doi.org/10.1111/j.1365-2133.2004.06129.x>
 46. Wallace VP, Woodward RM, Fitzgerald AJ, Pickwell E, Pye RJ, Arnone DA (2003) Terahertz pulsed imaging of cancers. Paper presented at the Proceedings of SPIE—the international society for optical engineering, vol 4949, pp 353–359. <https://doi.org/10.1117/12.500121>
 47. Wallace VP, Taday PF, Fitzgerald AJ, Woodward RM, Cluff J, Pye RJ, Arnone DD (2004) Terahertz pulsed imaging and spectroscopy for biomedical and pharmaceutical applications. *Faraday Discuss* 126(1):255–263. <https://doi.org/10.1039/b309357n>
 48. Walker GC, Berry E, Smye SW, Brett DS (2004) Materials for phantoms for terahertz pulsed imaging. *Phys Med Biol* 49(21):N363–N369. <https://doi.org/10.1088/0031-9155/49/21/N01>
 49. Wan M, Healy JJ, Sheridan JT (2020) Terahertz phase imaging and biomedical applications. *Opt Laser Technol* 122:105859. <https://doi.org/10.1016/j.optlastec.2019.105859>
 50. Wang M, Yang G, Li W, Wu Q (2013) An overview of cancer treatment by terahertz radiation. Paper presented at the 2013 IEEE MTT-S international microwave workshop series on RF and wireless technologies for biomedical and healthcare applications, IMWS-BIO 2013—proceedings. <https://doi.org/10.1109/IMWS-BIO.2013.6756170>
 51. Woodward R, Wallace VP, Pye RJ, Cole BE, Arnone DD, Linfield EH, Pepper M (2003) Terahertz pulse imaging of ex vivo basal cell carcinoma. *J Invest Dermatol* 120(1):72–78. <https://doi.org/10.1046/j.1523-1747.2003.12013.x>
 52. Woodward RM, Wallace VP, Cole BE, Pye RJ, Arnone DD, Linfield EH, Pepper M (2002) Terahertz pulse imaging in reflection geometry of skin tissue using time domain analysis techniques. *Proc SPIE Int Soc Opt Eng* 4625:160–169. <https://doi.org/10.1117/12.469785>
 53. Woodward RM, Cole BE, Wallace VP, Pye RJ, Arnone DD, Linfield EH, Pepper M (2002) Terahertz pulse imaging in reflection geometry of human skin cancer and skin tissue. *Phys Med Biol* 47(21):3853–3863. <https://doi.org/10.1088/0031-9155/47/21/325>
 54. Woodward RM, Wallace VP, Arnone DD, Linfield EH, Pepper M (2003) Terahertz pulsed imaging of skin cancer in the time and frequency domain. *J Biol Phys* 29(2–3):257–259. <https://doi.org/10.1023/A:1024409329416>
 55. Woodward RM, Fitzgerald A, Wallace VP (2004) Tissue classification using terahertz pulsed imaging. Paper presented at the Proceedings of SPIE—the international society for optical engineering, vol 5318, pp 23–33. <https://doi.org/10.1117/12.527477>
 56. Yang X, Zhao X, Yang K, Liu Y, Liu Y, Fu W, Luo Y (2016) Biomedical applications of terahertz spectroscopy and imaging. *Trends Biotechnol* 34(10):810–824. <https://doi.org/10.1016/j.tibtech.2016.04.008>
 57. Yin X, Hadjilucas S, Zhanga Y (2014) Complex extreme learning machine applications in terahertz pulsed signals feature sets. <https://doi.org/10.1016/j.cmpb.2014.06.002>
 58. Yu BL, Yang Y, Zeng F, Xin X, Alfano RR (2005) Reorientation of the H₂O cage studied by terahertz time-domain spectroscopy. *Appl Phys Lett* 86(6):1–3. <https://doi.org/10.1063/1.1862788>
 59. Zhao JW, He MX, Dong LJ, Li SX, Liu LY, Bu SC, Ouyang CM, Wang PF, Sun LL (2019) Effect of terahertz pulse on gene expression in human eye cells. *Chin Phys B* 28(4):048703. <https://doi.org/10.1088/1674-1056/28/4/048703>

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