Iranian Journal of Medical Physics

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IJMP

Detection of Melanoma Skin Cancer by Elastic Scattering Spectra: A Proposed Classification Method

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ARTICLE INFO

Article type:
Original Article

Article history:
Received: Jan 17, 2017
Accepted: Apr 23, 2017

Keywords:
Classification
Early Detection
Elastic Scattering
Spectroscopy
Melanoma

ABSTRACT

Introduction: There is a strong need for developing clinical technologies and instruments for prompt tissue assessment in a variety of oncological applications as smart methods. Elastic scattering spectroscopy (ESS) is a real-time, noninvasive, point-measurement, optical diagnostic technique for malignancy detection through changes at cellular and subcellular levels, especially important in early diagnosis of invasive skin cancer, melanoma. In fact, this preliminary study was conducted to provide a classification method for analyzing the ESS spectra. Elastic scattering spectra related to the normal skin and melanoma lesions, which were already confirmed pathologically, were provided as input from an ESS database.

Materials and Methods: A program was developed in MATLAB based on singular value decomposition and K-means algorithm for classification.

Results: Accuracy and sensitivity of the proposed classifying method for normal and melanoma spectra were 87.5% and 80%, respectively.

Conclusion: This method can be helpful for classification of melanoma and normal spectra. However, a large body of data and modifications are required to achieve better sensitivity for clinical applications.

► *Please cite this article as:*
Shirkavand A, Sarkar S, Fashtami L, Mohammadreza H. Detection of Melanoma Skin Cancer by Elastic Scattering Spectra: A Proposed Classification Method. Iran J Med Phys 2017; 14: 162-166. 10.22038/IJMP.2017.21367.1203.

Introduction

The global burden of cancer is constantly increasing largely due to aging and growth of the world population alongside with the growing adoption of cancer-causing behaviors, particularly smoking, in economically developing countries [1]. Skin cancers including basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma are common [2]. The mortality rate due to cutaneous malignant melanoma has grown over the past 20 years in most parts of the world [3-5]. Among the reasons for this trend, increased exposure to ultraviolet (UV) radiation as a result of lifestyle changes is generally recognized as an important factor [6].

Successful treatment of melanoma is contingent upon early diagnosis and excision [3]. Advancements in prognostic accuracy brings us closer to understanding the clinicopathologic events associated with metastasis, raising the likelihood of gaining new insight into possible cures [5, 7]. During the recent years, optical spectroscopy has become the basis for a wide range of research activities directed towards the development of novel, noninvasive technologies for tissue diagnostics [8].

Recently, elastic scattering spectroscopy (ESS) has been studied as a method for minimally invasive optical diagnosis of tissue pathologies, with emphasis on distinguishing dysplasia and cancer from normal tissue or benign conditions or for distinguishing different normal tissue types [9, 10]. ESS is a point measurement that is sensitive to the size and packing of dense subcellular components such as the nucleus, nucleolus, and mitochondria, as well as absorption by hemoglobin [9-13]. The size and density of these organelles change during transformation to premalignant or malignant conditions [10, 13-15]. ESS enjoys the advantage of being fast, reliable, and cost-effective and potentially offers a non-invasive, real-time, in situ diagnosis [13, 14, 16].

There have been several studies on ESS application in different fields of medical diagnosis such as skin cancer. A study was conducted to quantitatively assess the strength of correlation between ESS signal analysis

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for two wavelength ranges of ESS and histopathology in numerous cases suffering from melanoma [3]. There was also another in-vivo study comparing findings of ESS with histopathology, as a gold standard in patients with various skin lesions [17]. Since the ESS technology uses white light and produces a strong backscattered signal [16, 18], pattern recognition techniques and signal processing algorithms can be developed to classify spectra as benign, malignant, or normal tissues. The purpose of this study was to propose a classification method aiming to discriminate normal and melanoma skin ESS spectra.

Materials and Methods

As the setting of ESS was not available in our department, through collaboration with Biomedical Engineering Department of Boston University, some ESS spectra from their database (normal and melanoma) were sent to us that were already confirmed with histopathology (Figure 1). We used mean, as well as minimum and maximum of standard normal and cancerous spectra (four from each group) as the training signals, and analyzed other signals in comparison with the training signals. In total, 40 normal and melanoma signals (ESS spectra, 20 normal and 20 melanoma spectra) were included for the analysis of the program.

The spectral analysis and clustering of the normal and cancerous skin signals were carried out by means of a classification method developed in MATLAB (version 7.14, Mathworks Inc) using dimension reduction SVD-based, non-parametric, k-nearest neighbor (k-NN) analysis.

Dimension reduction plays a key role in constructing a discrimination model by reducing a large number of spectroscopic variables. There are some methods for dimension reduction including principle component analysis (PCA) and singular value decomposition (SVD). A difference between them is that SVD is robust against variations in intensity, while PCA is intensity-dependent [19]. Thus, in an actual experiment provided that the sample has enough signals to noise ratio (SNR), SVD is recommended [20].

Although there are some more sufficient, accurate dimension-reduction methods like manifold learning, here SVD-based algorithm was developed due to analysis of data as optical intensity versus wavelength spectra considered as linear dataset [21, 22]. The purpose of manifold learning is to map dataset from high-dimensional to low-dimensional, which is very effective in processing of high-dimensional or non-linear data [21]. In the current study, mainly SVD method, relying on some assumptions about the linearity of data (expected to be a linear combination of certain base vectors), was proposed [23, 24]. As several references, SVD solves linear systems with a general rectangular coefficient matrix. Singular value decomposition provides a convenient way for breaking a matrix, which perhaps contains some data we are interested in, into simpler, meaningful pieces [23]. In this study, SVD was used for dimension reduction to reduce a dataset while containing a large fraction of the variability present in the original data.

Classification, also known under the name of discriminant analysis or pattern recognition, is a class of methods primarily used to learn classification rules from training data belonging to known groups. These rules are later used on test data to assign new and unknown samples to the most probable groups.

K-NN analysis with five times repeat was used for clustering. K-means clustering is a method for classifying items into k groups (where k is the number of pre-chosen groups). The classification was performed by minimizing the sum of squared distances (Euclidean distances) in each cluster and the corresponding centroid. A centroid is "the center of mass of a geometric object of uniform density", though here, we considered mean vectors as centroids. For evaluation of the accuracy of classifying code, the sensitivity and specificity of the results were calculated as follows (table 1):

Sensitivity=TP/ (TP+FN)

Specificity=TN/ (TN+FP)

Accuracy= (TP+TN)/ (TP+FP+TN+FN)

In which: TP, FN, TN and FP are true positive, false negative, true negative and false positive respectively.

Table 1. Algorithm sensitivity and specificity for differentiating normal and melanoma elastic scattering spectroscopy spectra

Test result	Melanoma	Normal skin
Positive signal (1)	TP	FP
Negative signal (0)	FN	TN

TP: true positive, FN: false negative, FP: false positive, TN: true negative

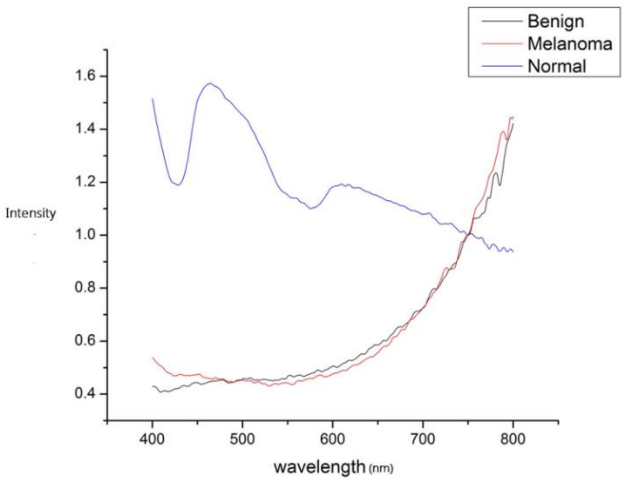

Figure 1. The elastic scattering spectroscopy spectra of melanoma, benign, and normal skin

Results

As already mentioned in the method section, dimension reduction was carried out by SVD method followed by K-mean clustering. Figure 2 presents the graphs of normal and melanoma spectra discrimination after running the program. One graph shows the melanoma spectrum clustering, while the other one is the graph of normal skin spectra. As this figure reflects, 16 out of 20 melanoma spectra were classified correctly. Regarding the detection of normal spectra, just one case was not classified in a correct way. Moreover, calculated specifity, sensitivity, and accuracy of the proposed method of classification was estimated and summarized in Table 2.

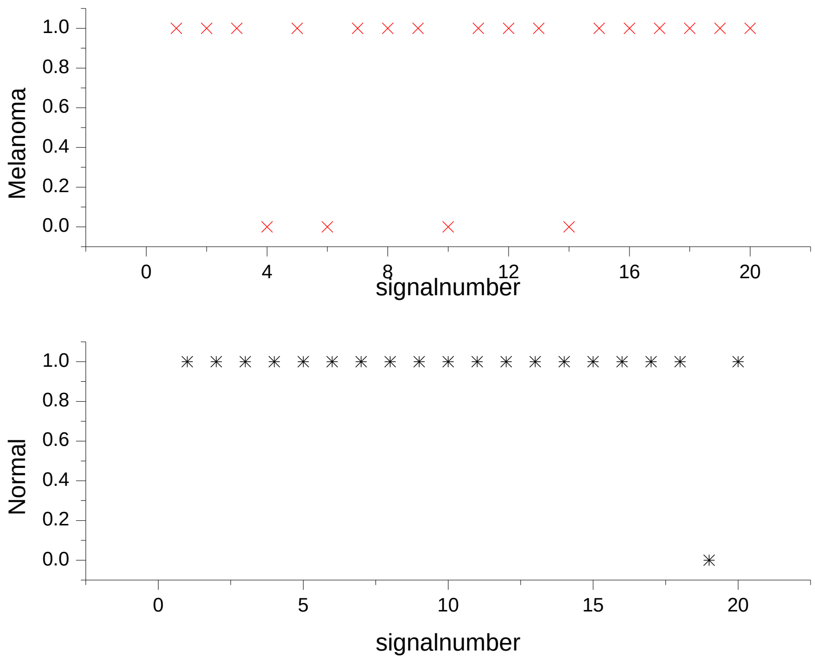

Figure 2. Results of normal and melanoma spectra discrimination

Table 2. Calculation of sensitivity and specificity

Statistical data	(%)
Sensitivity	80
Specifity	95
Accuracy	87.5

Discussion

The problems of skin cancer which is the most common type of cancer in the world, often arises from late diagnosis and subsequent resection [17]. Currently, the gold standard for assessing pathological changes in tissue is random biopsy followed by histopathology. However, the processing of biopsy material and interpretation of the results inevitably leads to delayed diagnosis and added possibility of taking an unrepresentative sample [17].

ESS, as a non-invasive, real-time, in-vivo optical diagnostic technique, is sensitive to alterations in the physical properties of human tissue. Since normal and abnormal tissues have different spectral patterns of scattering and absorption, it is possible to use acquired spectra to classify tissue lesions as normal or abnormal for the purpose of early detection of cancers [12, 18].

This optical diagnostic technique is a prompt and accurate way of examining tissue. The accuracy found in many of the previous studies suggests that it can provide cost-effective, real-time, and in situ diagnosis [17].

In this study, since we had not set-up the ESS system, we collaborated with Department of Biomedical Engineering of Boston University and received some ESS normal and melanoma spectra from their dataset that was previously confirmed histopathologically. The spectral analysis and clustering of the normal and cancerous skin signals were carried out by means of a classifying method, which was written in MATLAB applying SVD and k-NN analysis.

The results of running this code showed the accuracy of classification was 87.5% for differentiating normal and melanoma spectra (Table 2). However, considering small sample size of the data included in the study, sensitivity seems to be relatively low (80%). In a similar study conducted by Tahwinder Upile et al. in 2011, the data of BCC signals was analyzed based on linear discriminant analysis method. They reported a sensitivity of 77.8% and specificity 80.3% [17].

Since in melanoma screening it is vital to have highly sensitive technologies for early detection, it seems that the classification code needs some modifications to achieve higher sensitivity, especially for more accurate detection of melanoma. For this reason, we are performing additional surveys for developing a more sophisticated and accurate classification algorithm. In the near future, we are setting-up the system and collecting our standard melanoma and normal skin spectra as much as possible and analyzing them with classification code in order to achieve better sensitivity and accuracy.

A limitation of this study was that we did not have enough standard signals; thus, other studies for further signal acquisition from normal and melanoma skin and in-vivo and clinical studies followed by setting-up the ESS system are vital.

The advantages of SVD include managing the entire data analysis without taking into consideration the fundamental class structure, not requiring large computations, and having a rather simple geometric explanation, the singular value decomposition offers extremely effective techniques for putting linear algebraic ideas into practice. In contrast, for the feature of well-distributed classes in small datasets, it might not be considered as robust as other methods, which is considered as a disadvantage. All too often, a proper treatment in an undergraduate linear algebra course seems to be missing [22-24].

Conclusion

In conclusion, ESS, as a point measurement, real-time, noninvasive optical diagnostic technique beneficial for in-vivo and in-vitro studies, is sensitive to changes in the physical properties of human tissue. The results of this study presented the potency of classification method for discriminating melanoma skin spectra from normal ones following data acquisition by optical spectroscopy. However, our dataset was limited. We have more experiments and modifications on hand to improve the accuracy of discriminative algorithms.

Acknowledgment

This study was supported with a grant from Research Center of Science and Technology in Medicine (RCSTIM), Tehran University of Medical Sciences, Tehran, Iran.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics. 2013; CA Cancer J Clin. 2013 Jan; 63(1):11-30.
2. Murphy BW, Webster RJ, Turlach BA, Clay CJD, Heenan PJ., Sampson DD.toward the discrimination of early melanomafrom common and dysplastic nevus using fiber opticdiffuse reflectance spectroscopy. Journal of Biomedical Optics, 2005; 10:6, 0640201-9.
3. A'Amar OM, Ley RD, Bigio IJ. Comparison between ultraviolet-visible and nearinfraredelastic scattering spectroscopy of chemicallyinduced melanomas in an animal model. Journal of Biomedical Optics, 2004; 9(6), 1320–1326.
4. American Cancer Society. Cancer Facts & Figures 2016. Atlanta: American Cancer Society; 2016.
5. Garbe C, Peris K, Hauschild A, Saiag P, Middleton M, Bastholt L, et.al. Diagnosis and treatment of melanoma. European consensus-based interdisciplinary guideline e Update 2016. European Journal of Cancer, 2016; 63, 201-217.
6. Wang SQ, Setlow R, Berwick M, Polsky D, Marghoob AA, Kopf AW, Bart RS. Ultraviolet A and melanoma: A review. J Am Acad Dermatol, 2001; 44:837-46.
7. Day CL Jr, Mihm MC Jr, Lew RA, Kopf AW, Sober AJ, Fitzpatrick TB. Cutaneous Malignant Melanoma: Prognostic Guidelines for Physicians and Patients. CA-A cancer journal for clinician, 1982; 32: 2.
8. Bigio IJ and Mourant JR. Ultraviolet and visible spectroscopies for tissuediagnostics: fluorescence spectroscopy and elastic-scattering spectroscopy. Phys. Med. Biol, 1997; 42803–814.
9. Bigio IJ, Bown SG, Briggs G, Kelley, Lakhani S, Pickard D, Ripley PM, Rose IG, Saunders C. Diagnosis of breast cancer C.using elastic-scatteringspectroscopy: preliminary clinical results. Journal of Biomedical Optics, 2000; 5(2), 221–228.
10. Lovat LB, Bown SG. Elastic scattering spectroscopy for detection of dysplasiain Barrett's esophagus", gastrointestinal endoscopy clinicsof North America: optical biopsy, 14. Amsterdam: Elsevier, 2004; 507–17.
11. Mourant JR, Canpolat M, Brocker C .Light scattering from cells: thecontribution of the nucleus and the effects of proliferative status. J Biomed Opt, 2000; 5:131–7.
12. Zhu Y. Statistical aspects of elastic scattering spectroscopy with applications to cancer diagnosis. PhD thesis, Department of Statistical Science, National Medical Laser Centre, University College London, 2009.
13. Omar E, Current concepts and future of noninvasive procedures for diagnosing oral squamous cell carcinoma - a systematic review, Head & Face Medicine. 2015; 11:6.
14. Upile T, Jerjes W, Johal O, Lew-Gor S, Mahil J, Sudhoff H. A new tool to inform intra-operative decision making in skin cancer treatment: the non-invasive assessment of basal cell carcinoma of the skin using elastic scattering spectroscopy. Head Neck Oncol. 2012 Oct 31; 4(3):74.
15. Mourant JR, Hielscher AH, Eick AA. Evidence of intrinsic differences inthe light scattering properties of tumorigenic and nontumorigenic cells. Cancer, 1998; 84:366–74.
16. Sharwani A, Jerjes W, Salih V, Swinson B, Bigio IJ, El-Maaytah M, Hopper C. Assessment of oral

premalignancy using elastic scattering spectroscopy, Oral Oncology 42, 2006; 343–349.
17. Upile T, Jerjes W, Radhi H, Mahil J, Rao A, Hopper C. Elastic scattering spectroscopy in assessing skin lesions: An ''in vivo'' study. Photodiagnosis and Photodynamic Therapy 9, 2012; 132-141.
18. Dhar A, Johnson KS, Novelli MR, Bown SG, Bigio IJ, Lovat LB, Bloom SL. Elastic scattering spectroscopy for the diagnosis of colonic lesions: initial results of a novel optical biopsy technique. Gastrointestinal endoscopy, 2006; 63(2), 257-262.
19. Vaswani N and Guo H, Correlated-PCA: Principal Components' Analysis when Data and Noise are correlated, 30th Conference on Neural Information Processing Systems, NIPS 2016.
20. Oblefias1WR., Soriano MN, Saloma CA. "SVD vs. PCA: Comparison of Performance in an Imaging Spectrometer. Science Diliman. 2004; 16:2, 74-78.
21. Golchin E, Maghooli K, Overview of Manifold Learning and Its Application in Medical Data set, International journal of Biomedical Engineering and Science (IJBES), Vol. 1, No. 2, July 2014.
22. Karamizadeh S, Abdullah SM, Manaf AA, Zamani M, Hooman A, An Overview of Principal Component Analysis, Journal of Signal and Information Processing, 2013, 4, 173-175.
23. Kalman D, A Singularly Valuable Decomposition: The SVD of a Matrix, The College Mathematics Journal 27 (1996), 2-23.
24. Petrıcek M, Components in Data Analysis, WDS'10 Proceedings of Contributed Papers, Part I, 82–87, 2010.