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● *Original Contribution*

QUANTITATIVE SONOGRAPHY OF BASAL CELL CARCINOMA

Hanna Piotrzkowska-Wroblewska,* Jerzy Litniewski,* Elzbieta Szymanska,† and Andrzej Nowicki*

*Department of Ultrasound, Institute of Fundamental Technological Research, Warsaw, Poland; and †Dermatology Clinic, CSK MSWiA Hospital, Warsaw, Poland

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Abstract—A 30-MHz ultrasonic scanner was used to collect B-scan images together with appropriate radiofrequency echoes from diseased and healthy skin regions of patients with diagnosed basal cell carcinoma and pre-cancerous lesions (actinic keratosis). Radiofrequency data were processed to obtain the attenuation coefficient and statistics of the backscattered echo signal determination (K-distribution and effective density of scatterers [EDS]). The attenuation coefficient was significantly higher for patients with basal cell carcinoma than for healthy patients. Also, the pre-cancerous skin lesions had increased attenuation. The averaged EDS values for cancer lesions were significantly lower than those for pre-cancerous lesions and healthy skin. The successful differentiation between the tissue groups examined suggests the potential value of the attenuation coefficient and EDS for carcinoma characterization. (E-mail: hpiotrzk@ippt.pan.pl) © **2015 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Quantitative ultrasound, High frequency, Human skin, Skin lesions, K-distribution, Attenuation coefficient, Tissue characterization.**

INTRODUCTION

Basal cell carcinoma (BCC) is the most common cutaneous malignancy, representing 80% of all skin cancer cases. BCC arises from the basal cells of the epidermis. Although BCC is not associated with significant mortality, the associated morbidity and therapeutic costs are an increasing burden to the health care system. BCC cases are rather easily diagnosed, but a substantial number of cases require biopsy because of their similarity to other cutaneous neoplasms, both benign and malignant, making the BCC direct diagnosis ambiguous.

Basal cell carcinoma can develop from pre-cancerous growths like an actinic keratosis (AK), as well as from unchanged skin. According to Cham (2013), it is estimated that up to 50% of the population is affected by AK. The difficulty in predicting the evolution of this kind of lesion makes AK very dangerous. It may not be a threat to the health and life of the patient for a long period, but at some point it can vanish or transform into cancer.

Address correspondence to: Hanna Piotrzkowska-Wroblewska, Department of Ultrasound, Institute of Fundamental Technological Research, ul. Pawinskiego 5 b, 02-106 Warsaw, Poland. E-mail: hpiotrzk@ippt.pan.pl

Foster et al. (2000) reported that although ultrasound (US) has the capability to image fine features in the skin, such as sweat gland ducts, hair follicles and veins, the diagnostic ability of skin images to reveal specific pathologies is limited. It is difficult to differentiate between benign and malignant lesions using B-scan images (Fornage et al. 1993) because both types of lesions appear hypo-echogenic compared with healthy skin. Another study indicated that both scar tissue and malignant melanoma could appear similar in US scans (Turnbull et al. 1995). Thus, biopsy is still the gold standard in final diagnosis of skin cancer; however, quantitative ultrasound can provide additional information that is potentially helpful in lesion assessment and screening tests.

First, quantitative studies of skin lesions *in vivo* using ultrasound have mostly been limited to parameters that could be computed directly from images, recorded by using commercially available 20-MHz systems. For instance, changes in skin echogenicity (mean pixel amplitude, which is proportional to the mean backscatter amplitude) and skin thickness have been found to be related to photo-aging of the skin (Gniadecka and Jemec, 1998). The degree of acoustic shadowing, measured as the ratio of echogenicity of the retrocessional dermis to that of the perilesional dermis, was found to be

capable of differentiating between basal cell papilloma and malignant melanoma (Harland et al. 2000). Other parameters that require analysis of radiofrequency (RF) backscattered echoes, such as the attenuation coefficient (Guittet et al. 1999) and the apparent integrated backscatter (Fournier et al. 2001), have also been studied in healthy skin tissues *in vivo*.

Although the statistics of ultrasonic signals have been extensively studied with respect to their potential to classify tissue types (Shankar et al. 1993, 2000; Tsui et al. 2010), such studies have not been widely carried out in skin tissue. Raju and Srinivasan (2001, 2002) studied *in vivo* the frequency-dependent attenuation and backscatter coefficient, as well as parameters related to echo statistics, such as the ratio of mean to standard deviation, denoted as signal-to-noise ratio (SNR), and the parameters of envelope probability density functions (PDFs) of healthy skin tissues. They found that the generalized gamma, K- and Weibull distributions modeled the envelope statistics well, whereas the Rayleigh distribution provided a rather poor fit.

The use of quantitative ultrasound in the monitoring of skin tissue affected by basal cell carcinoma was proposed by Petrella et al. (2012). Their study was performed *ex vivo* using an ultrasound biomicroscope working at a frequency of 45 MHz. They examined SNR and shape parameters of Weibull and generalized gamma PDFs. The significant differences between lesions with various distribution patterns of tumor nests suggested that quantitative ultrasound has potential for use in carcinoma characterization.

Similar results were presented in our previous study. We found that the K-distribution is appropriate for modeling statistics of the envelope of signals obtained from human skin *in vivo*, and the value of the shape parameter of the K-distribution can help in differentiation of healthy skin and skin affected by BCC (Piotrzkowska et al. 2012).

The goal of this study was to find the quantitative measure of skin tissue backscattering properties for differentiating changes in tissue structure induced by BCC and AK. The new method allows non-invasive differentiation of the disease entities and, consequently, selection of the proper method of treatment. In the case of BCC, the most common method of treatment is surgical removal of lesions with the correspondingly large margin or, in some cases, cryotherapy or laser therapy. Actinic keratosis requires conservative treatment, locally (imiquimod or isotretinoin) or with cryotherapy or laser therapy. Because the recorded signals are dependent on both the tissue properties and the instrument used in recording the signals, methods for computing quantitative parameters, such as the attenuation coefficient and the shape parameter of the K-distribution, were investigated, taking into account the compensation of the influence of the system-dependent effects.

STRUCTURE OF HUMAN SKIN AND BBC LESIONS

Skin is a multilayered organ, with the separate histologic layers epidermis, dermis and subcutaneous tissue. The epidermis is the thinnest layer of skin. The main cell populations of the epidermis are keratinocytes, melanocytes and Langerhans cells. The middle layer of skin is the dermis, which consists of connective tissue arranged in two layers: the more superficial papillary dermis and the deeper reticular dermis. Thin papillary dermis is made of loose connective tissue containing mostly collagen fibers. In the thicker reticular dermis, connective tissue is denser because of the coarse bundles of collagen fibers arranged in layers parallel to the skin surface. There are other structures in the dermis, such as blood vessels, lymphatic vessels, nerve fibers, portions of hair follicles and sweat glands; however; their volume percentage is much lower than that of collagen fibers. All dermal components are bound together by a gel-like ground substance made of various glyosaminoglycans and glycoproteins. The third skin layer is subcutaneous fat, further divided into lobules containing adipose cells and separated by thin fibrovascular septa. The septa consist of collagen and reticulin fibers, blood and lymphatic vessels and cutaneous nerves.

Basal cell carcinoma tumors are typically characterized by a fibrous stroma surrounding clusters of tumor cells that resemble collagen fibers of the basal layer of the epidermis. Usually, these tumor cells are fairly regular with rounded nuclei and little cytoplasm. The level of skin changes (percentage of pathologic structures in the volume of tissue) reflects the progression of the lesion. In the initial phase of the disease, the number of cancerous cells is relatively low; however, in the advanced stage of cancer, the number and size of clusters increase, which reduces the proportion of collagen fibers in the dermis to about 30%.

In 30-MHz ultrasonic images, all three layers of skin can be observed. BCC lesions are usually located in the dermis, and all results discussed in this article concern this layer. The echogenicity in images of the dermis is determined by a collagen component (Wortsman and Jemec 2013).

Collagen fibers are 5–15 μm thick with an average density of 1250 kg/m^3 and longitudinal wave sound speed of 1730 m/s (Weber et al. 1984) Thus, the resultant impedance is much higher than the impedance of BCC cells. We assume that the replacement of fibers by tumor cells leads to changes in tissue attenuation and backscatter statistics.