Virtual biopsies of tissues and carcinomas using vibrational optical coherence tomography

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Abstract

Vibrational optical coherence tomography (VOCT) is a new technique that combines the imaging power of optical coherence tomography with the use of sound to characterize the physical properties of tissues. This technique has been developed to perform "virtual" biopsies and biomechanical measurements on normal and malignant tissues non-invasively and non-destructively. It has been previously reported that cutaneous wound healing and the development of malignant skin lesions are associated with changes in tissue stiffness. VOCT produces images of groups of cells as well as biomechanical information in three dimensions that can distinguish normal from pathological tissue. In addition, the biomechanical properties of the tissue margins can be characterized. The images and the biomechanical data from measurements made on different skin lesions and carcinomas together can help plan surgical interventions and monitor the healing process of skin lesions. VOCT produces images of groups of cells as well as measurement of the tissue resonant frequency in three dimensions which assists in distinguishing normal from pathological tissue. We have imaged and studied several types of skin lesions including a BCC, SCC Actinic Keratosis and a Nevi using VOCT to evaluate the morphology, stiffness, depth and margins of these structures. While cellular components present in skin and carcinomas have resonant frequencies in the range of 30 to 60 Hz, normal collagen has a resonant frequency in the range greater than 90 Hz. In comparison, fibrotic collagen is shown to have resonant frequencies above 150 Hz as does collagen from skin lesions. It is concluded that the ratio of the resonant frequency squared to the tissue thickness obtained from VOCT can be used to grade the type of tissue response seen. Further studies are underway to establish the relationship between tissue stiffness and lesion morphology for cellular and fibrotic lesions based on the characteristic ratios of resonant frequency and tissue thickness. The results therefore suggest that the antioxidant supplement might have a restorative effect on kidney function and also enhance effective electrolyte balance and control for easy movement of ions across cell membrane. Previous literature reports suggest that tissue stiffness is a predictor of cancer and metastatic behavior. We have used optical coherence tomography and vibrational analysis (VOCT) to characterize normal skin, scar and a verrucous carcinoma, a squamous cell carcinoma subtype, non-invasively and non-destructively. The results suggest that epidermal thickening and increased keratin production occur in verrucous carcinoma and lead to increases in surface hills and valleys as well as subsequent increases in epidermal stiffness values. Increased stiffness of the epidermis is a result of increased keratin production while the stiffness of the dermis remains similar to that of normal skin, suggesting that dermal changes are not observed in this lesion. It is concluded that VOCT may ultimately be a useful adjunct to dermoscopy and other clinical tools to identify and characterize lesions as small as 0.2 mm. It is hypothesized that the slow growth potential of verrucous carcinoma may be related to the lack of dermal involvement and that other more invasive skin lesions may be characterized by both epidermal and dermal involvement that would lead to changes in both epidermal and dermal stiffnesses. Background Increased tissue stiffness (also termed modulus) has been shown to be a characteristic of potential tumor metastasis. Measured values of the stiffness of tumors and cancer cells are reported in the literature to increase compared to neighboring normal tissues. Yet the relationship between the mechanical properties of cells and the extracellular matrix has yet to be correlated with the histopathology of cancerous lesions. Materials and Methods We have developed a technique to do virtual biopsies of skin lesions by combining images made using optical coherence tomography with stiffness measurements made simultaneously using vibrational analysis. The technique is termed vibrational optical coherence tomography (VOCT).

Results In this paper, we report that precancerous and cancerous lesions are characterized by changes in both the morphology and stiffness of the cellular components of the skin. The ratio of the peak heights that correspond to the epidermal (40-60Hz) and dermal (140-160 Hz) resonant frequencies appear to be different for benign and cancerous or precancerous lesions compared with normal skin and scar. Conclusions Cell-to-cell and epidermal-to-dermal interactions may be very important in evaluating the potential of skin lesions to become malignant. These interactions can be evaluated using VOCT, a new technique for performing "virtual biopsies" of skin lesions. Increased tissue stiffness (also termed modulus) has been shown to be a characteristic of potential tumor metastasis. Measured values of the stiffness of tumors and cancer cells are reported in the literature to increase compared to neighboring normal tissues. Yet the relationship between the mechanical properties of cells and the extracellular matrix has yet to be correlated with the histopathology of cancerous lesions. Materials and Methods: We have developed a technique to do virtual biopsies of skin lesions by combining images made using optical coherence tomography with stiffness measurements made simultaneously using vibrational analysis. The technique is termed vibrational optical coherence tomography (VOCT). Results: In this paper, we report that precancerous and cancerous lesions are characterized by changes in both the morphology and stiffness of the cellular components of the skin. The ratio of the peak heights that correspond to the epidermal (40-60Hz) and dermal (140-160 Hz) resonant frequencies appear to be different for benign and cancerous or precancerous lesions compared with normal skin and scar. Conclusions: Cell-to-cell and epidermal-to-dermal interactions may be very important in evaluating the potential of skin lesions to become malignant. These interactions can be evaluated using VOCT, a new technique for performing "virtual biopsies" of skin lesions.

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