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Spontaneous photon emission: A promising non-invasive diagnostic tool for breast cancer

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ABSTRACT

Ultra-weak photon emission (UPE) has attracted significant scientific attention for its potential to monitor the physiological and pathological characteristics of living systems. In this study, we investigated the strength of spontaneous photon emission (SPE) from the right (R) and left (L) side of body surface of human breast cancer-bearing nude mice models, considering the entire breast cancer growth process, and healthy controls using a photon detector. And then we calculated the ratio of the average SPE strength (ratio (R/L)) between the right and left side of each mouse. Cluster analysis was used to evaluate the accuracy rates of strength-R, strength-L, ratio (R/L) and their combination to identify tumor mice from the controls. Our results revealed that the discriminating powers of different parameters were different in different growth stages of tumor: in tumor incubation period, the accuracy rates of strength-R, strength-L, ratio (R/L) and their combination to identify tumor mice from control mice were 63.6%, 40.9%, 81.8% and 86.4%, respectively; For nude mice with tumor diameter <0.5 cm, the accuracies were 72.7%, 45.5%, 86.4% and 90.9%; and for nude mice with tumor diameters larger than 1.5 cm, the accuracies were 86.4%, 77.3%, 95.5% and 100%, respectively. These results indicated that the SPE from the body surface of the lesion site could significantly distinguish tumor mice from the controls when tumors were obvious or when there were no obvious morphological changes, although the accuracy was relatively low. The results suggest that SPE, as a sensitive and promising optical method, may contribute to the preliminary screening of breast cancer, especially for early diagnosis, and it may play a critical role in curtailing the effects of breast cancer and improving the survival of patients in the future.

1. Introduction

All living things spontaneously emit ultra-weak photon emission (UPE), often called biophotons, mainly in the visible region [1]. Spontaneous ultra-weak photon emission (SPE) is an intrinsic attribute of biological systems originating from the relaxation of electronically excited species formed in biological systems during normal or abnormal oxidative metabolic processes [2,3]. Oxidative metabolic processes are the fundamental chemical reactions that sustain life in biological systems, and small changes in living organisms cause changes in metabolism, leading to changes in SPE. Therefore, SPE has many unusual features. It can reflect the overall physiological and pathological conditions of living organisms. As a result, the measurement of SPE as a novel and non-invasive method has attracted considerable attention in monitoring the state of living organism and has been used in many fields, such as agriculture [4,5], detection of food quality [6], evaluation of medicinal properties of herbs [7], assessment of cancer cells or tissues [8–11] and some other health problems [12–16].

Breast cancer is the most common type of cancer in women worldwide and presents the greatest health care challenge in today's world. Despite the vast knowledge of the disease, its incidence has never shown a declining trend. If it can be detected and diagnosed in a nearly stage, breast cancer is one of the most treatable forms of cancer. Thus, early detection and diagnosis is the best way to curtail the effects of this disease and to improve patient survival. Currently, the imaging methods under development for the early diagnosis of breast cancer include ultrasound, X-ray mammography and magnetic resonance imaging. Although the three techniques can provide high spatial resolution, relatively little information about the molecular-level changes of the breast tissue is provided [17–19]. In addition, it is difficult to detect abnormal lesions before morphological characteristics are obvious. For example, according to the National Cancer Institute, up to 10% of all breast

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cancers, approximately 20,000 cases per year in the United States, fail to be discovered by X-ray mammography [20]. Additionally, X-ray mammography uses ionizing radiation, which has a killing effect on normal somatic cells. Therefore, X-ray mammography should not be used in early medical screening for normal people <35 years old, and X-raymammography should not be performed >1 time per year. Accordingly, it is of great significance to develop a novel detection method as an aid and supplementary diagnostic tool for preliminary screening that is not only non-invasive but also is of sufficient sensitivity and provides some metabolism information about the physiological and pathological conditions of the breast tissue. It is in this setting of the diagnostic dilemma of breast diseases that SPE may have potential.

There are many reports on the relationship between biophoton emission and human cancer. For example, by measuring SPE during human carcinoma cell culture proliferation, Motohiro Takeda et al. found that the intensity of SPE mainly depended on the cell population, and they suggested that SPE had a potential role in cancer diagnosis [21]. Hwan-Wook Kim et al. measured biophoton emission from human cancerous lung tissue and adjacent normal lung tissue and found that biophoton emission could be used to differentiate the tumor from adjacent normal tissue and also showed a salient difference between squamous cell carcinoma and adenocarcinoma [9]. Serum samples were successfully used by Chen et al. to distinguish patients with acute lymphoblastic leukemia from healthy volunteers [12]. In addition, a comparison was performed by Jungdae Kim et al. in 2006 between the intensities of biophoton emission from tumor-bearing mice transplanted with ovarian cancer cells and control mice, and the difference was significant [22]. These studies demonstrated that the measurement of SPE could be considered as a novel and promising optical method for the diagnosis of cancer.

However, most studies focused on tumor cells, tissues or sera and few studies investigated the changes in biophoton emission from the surface of subjects with cancer compared to healthy subjects. In addition, there are no reports on the characteristics of biophoton emission from the body surface of abnormal lesions before morphological characteristics were obvious. Therefore, we conducted research based on previous reports to investigate on the characteristics of SPE from the body of a human breast cancer-bearing nude mouse model, considering the overall growth process (from transplantation into nude mice to growth into a large tumor) of breast cancer using a sensitive photomultiplier tube (PMT). By comparing and analyzing the data, an interesting and meaningful result was found: SPE not only was used to distinguish tumor mice from the health ones but also could be used to predict the occurrence of tumors, even without an obvious morphological change. These results indicated that SPE measurement may play a critical role in preliminary breast cancer screening or at least be a novel, non-invasive, supplementary method for the early diagnosis.

2. Materials and Methods

2.1. SPE-Detection System

The schematic representation of the SPE-detection system used in our study is shown in Fig. 1. The main components of this system include a PMT, PMT housing for cooling, high voltage power supply, shutter system, photon-counting unit, sample stage, moveable frame, control box and a computer with photon-counting software. The control box and computer are placed in the operation room to facilitate tester operation, and the remaining parts of the system are placed in a special darkroom to ensure magnetic and light shielding. As the core component of the detection system, the PMT (ET Enterprises, Britain, 9235QA) is installed on a moveable frame. In this way we can conveniently adjust the detection position of the nude mice and ensure the distance between the detection site and the PMT window is the same for all measurements. A shutter system is placed in front of the PMT to eliminate the disturbance of external light.

SPE from the nude mice was detected by the highly sensitive and low-noise PMT in single-photon-counting mode with a spectral response ranging from 290 nm to 630 nm. The photons were processed by the photon-counting unit and fed into the computer with photon-counting software. To increase the sensitivity and decrease the dark current, the PMT was cooled to −23 °C using FACT50 PMT cooling housing (ET Enterprises, Britain). A sample holder was placed in the darkroom to

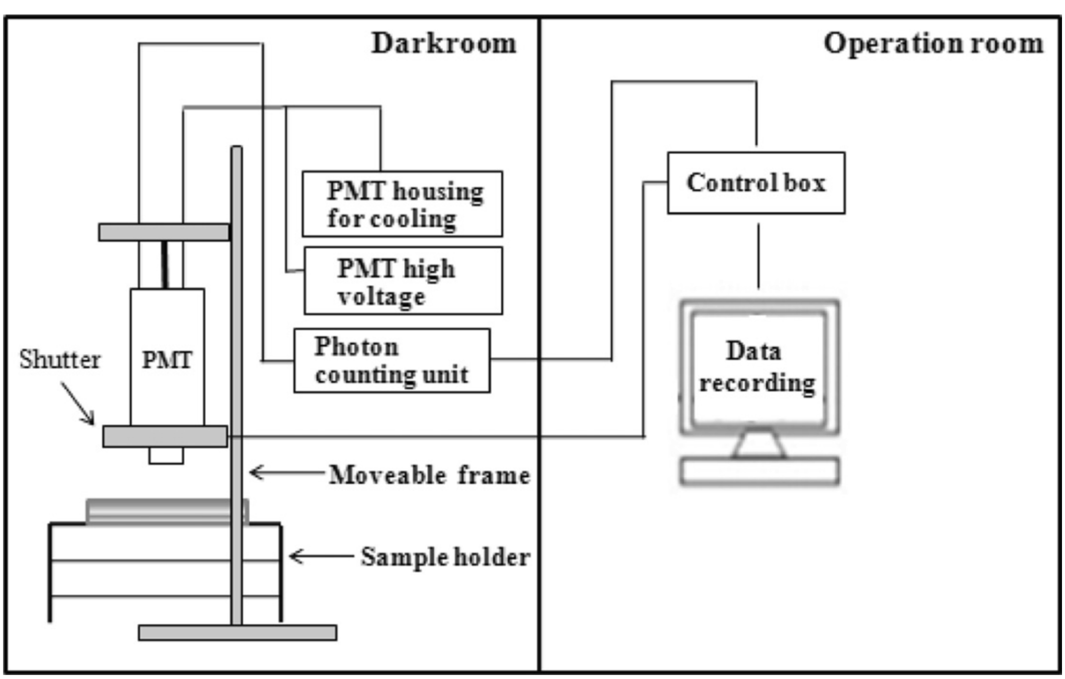

Fig. 1. The schematic representation of the biophoton detection system used in this study.