ABSTRACT

Laboratory animals provide important models for studying human diseases, including many types of cancer. Mice are among the most commonly used laboratory animals, allowing for the study of carcinogenic agents, cancer development and for testing innovative preventive and therapeutic strategies. Thus, monitoring angiogenesis in animal models is a major goal for cancer research. Among the currently available imaging techniques, thermography is a useful approach for studying the superficial vascularization of cancer, based on their heat emissions. At this chapter emphasis is placed on thermography and its applications on laboratory animals, in comparison with other available and applicable imaging techniques. In conclusion, thermography may be usefully applied to the study of cancer vascularization in animal models, particularly when using laboratory rodents such as mice. Care is needed in adapting existing approaches to the specificities of each animal species.
INTRODUCTION

Among the major public health problems of our time, cancer occupies a prominent place. Cancer develops through a complex, multistage process, driven by the cellular accumulation of genetic mutations and epigenetic events (Bignold, 2003; Bignold, Coghlan, Jersmann 2006; Oliveira et al., 2007; Iacobuzio-Donahue, 2009). This process of carcinogenesis often proceeds through multiple distinguishable morphological stages as shown in Figure 1. Thus, pre-cancerous lesions may develop into benign and later malignant tumors. The term cancer is reserved for malignant lesions, while the term neoplasia (used of a tissue which has become independent of normal physiological regulatory mechanisms) applies to both benign and malignant tumors. Hence, early non-tumoral lesions are often referred to as pre-neoplastic. Environmental carcinogens are biological (e.g. human papillomavirus, HPV), chemical (e.g. nitrosamines) or physical (e.g. ionizing radiations) agents that initiate carcinogenesis by inducing genetic mutations or promote it otherwise (Oliveira et al., 2007). Genetic mutations occurring in healthy cells are, most often, successfully repaired or else they trigger programmed cell death mechanisms (as a way to prevent carcinogenesis). However, unrepaird mutations that block DNA repair mechanisms (encoded by so-called tumor suppressor genes) will promote the unchecked accumulation of further mutations (genomic instability). Mutations that activate genes (so-called proto-oncogenes) that contribute to make the cell independent from its environment (e.g. by producing its own growth factors) are also important in driving carcinogenesis. Accordingly, during the early phases of carcinogenesis, cells tend to survive and proliferate in an unregulated fashion, accumulating additional mutations (Oliveira et al., 2007) that will drive carcinogenesis further on Figure 1. As already pointed out, neoplastic tissues are not necessarily malignant. While benign tumors are well-delimited and damage adjacent tissues mainly by compressing them, malignant tumors (cancers) are able to invade adjacent tissues or event to spread to distant body parts through lymphatic or blood vessels. Progression from a benign to a malignant stage is commonly observed in many epithelial tumors. The malignant phenotype requires an ability to interact with and invade the adjacent connective tissue (called the stroma). When neoplastic cells have acquired the typical traits of malignancy, they degrade the basement membrane that separates them from the stroma, and spread into the adjacent tissues. By invading blood and lymphatic vessels (a phenomenon called intravasation) in the stroma, malignant cells may gain access to distant organs, where they may establish distant tumor foci, called metastasis. The interaction between malignant or pre-malignant cells and the adjacent stroma is highly complex.

In order to study these phenomena, researchers have long resorted to employing animal models, which allow for fast and efficient experimental approaches. Thermography, as an imaging technique, is able to provide valuable additional information on the physiology and pathology of these models, namely concerning superficial inflammation and blood irrigation. The present chapter deals with laboratory animal models of cancer, followed by multiple imaging techniques available for use in these models. Special emphasis is given to the use of thermographic techniques to evaluate laboratory mice and rats.

ANGIOGENESIS IN CANCER

One key feature of the interaction between cancer cells and their adjacent stroma is the development of new, and often abundant, blood vessels, termed angiogenesis (Potente, Gerhardt, Carmeliet, 2011). Tumor-associated angiogenesis is of particular importance clinically and also from the viewpoint of
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