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ORIGINAL ARTICLE

A new semiquantitative method for evaluation of metastasis progression

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Summary

Purpose: *Although recent technical advancements are directed toward developing novel assays and methods for detection of micro and macro metastasis, there are still no reports of reliable, simple to use imaging software that could be used for the detection and quantification of metastasis in tissue sections. We herein report a new semiquantitative method for evaluation of metastasis progression in a well established 4T1 orthotopic mouse model of breast cancer metastasis.*

Methods: *The new semiquantitative method presented here was implemented by using the Autodesk AutoCAD 2012 program, a computer-aided design program used primarily for preparing technical drawings in 2 dimensions.*

Results: *By using the Autodesk AutoCAD 2012 software-aided graphical evaluation we managed to detect each metastatic lesion and we precisely calculated the average percentage of lung and liver tissue parenchyma with metastasis in 4T1 tumor-bearing mice. The data were highly specific and relevant to descriptive histological analysis, confirming reliability and accuracy of the AutoCAD 2012 software as new method for quantification of metastatic lesions.*

Conclusion: *The new semiquantitative method using AutoCAD 2012 software provides a novel approach for the estimation of metastatic progression in histological tissue sections.*

Key words: cancer, metastasis, method, quantification

Introduction

Metastasis is defined as the spread of cancer cells from a primary site resulting in the establishment of secondary tumors in distant locations [1,2]. The metastatic process is comprised of a series of complex and sequential steps which cancer cells have to successfully complete in order to give rise to a metastatic tumor [1-4]. These steps are: i) intravasation (escape from the primary tumor); ii) dissemination (via the blood or lymphatic system) and survival within the circulation; iii) arrest and extravasation into a secondary site; iv) initiation of growth into micrometastases; and v) maintenance of growth as vascularized, clinically detectable macrometastases [1-4]. Metastasis is the primary cause of death from breast cancer, the most common form of cancer affecting women in the United States, and the second leading cause of cancer-related deaths in women around the world [1]. Certain types of cancers have organ-specific preferences for metastatic growth [1]. However, most of cancer cells usually metastasize to the lungs and liver, making these metastases the leading cause of death for cancer patients [5-7]. In particular, breast cancer cells display a predilection for metastasis to lungs, liver, bone, brain and regional lymph nodes [1,4,8-11].

Opportunities to improve outcomes of cancer patients require a greater understanding of the biology of the metastatic process. *In vitro* analysis of the metastatic process is not sufficient to mimic the complex interaction between cancer cells and the surrounding microenvironment that is crucial for metastasis in humans [7]. On the contrary, *in vivo* models of metastasis, largely in mice, are developed with an aim to provide end points of the metastatic outcome (i.e., presence or absence of metastasis) and time to late-stage metastatic events [7].

The 4T1 mammary carcinoma cell line, originally isolated by Fred Miller and coworkers at the Karmanos Cancer Institute [12,13], when introduced orthotopically is an useful experimental model for the evaluation of breast cancer metastasis [14]. The 4T1 tumor cell line

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