



# Is software method helpful for detection of angiogenesis in breast tissue slides?

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## Core tip

Sustained angiogenesis is a hallmark of solid tumors. Nowadays, a lot of studies are conducted to investigate angiogenesis and angiogenic pathways. There are many anticancer agents targeting these pathways. However, there is not a clinical method to detect or quantify angiogenesis. In ImageJ software, color threshold of angiogenesis can be defined. However, this method is not specific for hematoxylin and eosin stained slides.

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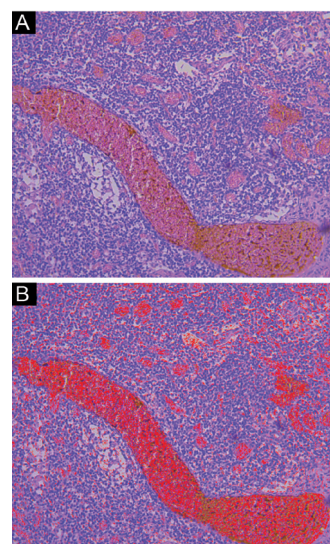


Sustained angiogenesis is a hallmark of solid tumors. It means that cancer cells secrete angiogenic factors to access the body circulation. Therefore, the tumor can be survived and spread. Several factors are associated with induction of angiogenesis such as hypoxia and inflammation (1, 2). Oxidative stress is associated with more angiogenesis and epithelial to mesenchymal transmission (3). Breast cancer is the most common solid tumor in women. The most common malignant tumor of breast is invasive ductal carcinoma (4) and the most benign tumor of breast is fibroadenoma (5).

Nowadays, a lot of studies are conducted to investigate angiogenesis and angiogenic pathways. There are many anticancer agents targeting these pathways (6). However, there is not a clinical method to detect or quantify angiogenesis. A simple and low-cost method is to study hematoxylin and eosin (H&E) stained slides of tumors by software. Therefore, we conducted a study on the slides of breast cancer, breast fibroadenoma and breast normal tissues.

The Java-based program ImageJ (provided by National Institute of Health, Fiji version) was used. Color thresholds were defined for red blood cells (RBC) and vessel sections based on a lymph node slide because of more

obvious angiogenesis. According to this, the color threshold for RBCs was defined as 13-26 and the color threshold for vessel sections was defined as 220-255 (Figure 1). The percentage of the color between the thresholds interval was calculated (Table 1). Receiver operating characteristics (ROC) curve showed that the method is not a diagnostic tool for detection of malignant



**Figure 1.** Defining color threshold in slide of an axillary lymph node. A) Before using threshold; B) after using threshold.

**Table 1.** Percentage of color threshold intervals in some slides

Code	Group	Threshold (13-26) %	Threshold (220-255) %
#1	Cancer	0.860	4.073
#2	Cancer	0.993	3.063
#3	Cancer	1.27	3.554
#4	Cancer	0.750	9.331
#5	Cancer	0.304	12.079
#6	Cancer	1.330	10.796
#7	Cancer	0.132	3.517
#8	Cancer	0.307	1.660
#9	Cancer	1.581	15.113
#10	Cancer	3.325	8.131
#11	Cancer	1.104	15.450
#12	Benign	0.062	0.625
#13	Benign	0.249	1.877
#14	Benign	0.446	4.144
#15	Benign	1.490	6.233
#16	Benign	0.753	6.499
#17	Benign	0.981	12.853

and benign tissues of breast (Figure 2).

The present method can be used as a nonspecific tool for detection of angiogenesis. However, its diagnostic accuracy should be studied in further examples. Other software such as Motic Image Plus can also be used. Using more specific staining methods may be helpful, because H&E staining is not accurate enough.

#### Authors' contribution

SS; sample collection and clinical consult. MP; pathological study of the slides. RN; design and manuscript draft. All authors read and signed the final paper. SS; bioinformatics and analysis consult.

#### Conflicts of interest

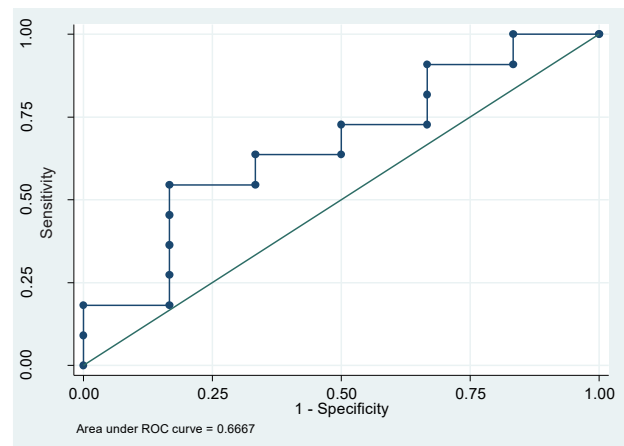
The authors declare that there is no conflict of interest.

#### Ethical consideration

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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**Figure 2.** ROC curve analysis for diagnostic accuracy of using angiogenesis color threshold for detection of malignant breast tissues.

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