Application Note: Validating New Modalities for Breast Cancer Research

Introduction

Breast cancer is the leading type of cancer affecting women worldwide. In 2013, there were an estimated 232,340 new cases and 39,620 deaths in the United States alone. Treatment typically involves surgery to remove part or all of the breast, followed by chemotherapy and/or radiation therapy. Although early detection methods have improved in recent years, many women are still diagnosed with locally advanced breast cancer (LABC), a late stage of the disease, which results in a poorer long-term chance of survival. In these cases, patients are given more aggressive *neo-adjuvant* therapy, administered weeks and months prior to surgery. While a response to neo-adjuvant therapy has been correlated to improved chances of survival, uncertainties regarding the choice of treatment and its duration make it a controversial method. The sooner oncologists can see a patient's response to neo-adjuvant therapy, the sooner they can provide an alternative therapy if necessary, improving chances of survival. Therefore early detection of responses to treatment and individualized medicine are two key areas of current breast cancer research.

Towards these ends, new imaging techniques are showing promise for detecting early responses to therapy. Traditionally, anatomical measurements such as physical assessment, mammography, and ultrasound have been used to assess a patient's response to therapy; however, tumors may take months to reduce in size, even when patients respond well to treatment.

On the other hand, if oncologists are able to see a tumor's physiology, they can detect a response to treatment much earlier, potentially within a week. Hence non-invasive techniques such as quantitative ultrasound, ultrasound elastography, and diffuse optical spectroscopy (DOS) are imaging modalities which are being demonstrated to indicate early responses to therapy.

But how do researchers validate these new techniques and prove that they have translational value to cancer care at large? Researchers must prove that an imaging method predicts an ultimate clinical and pathological response, and so in studies on quantitative ultrasound, elastography, and DOS techniques, breast tissue specimens are mounted on slides post-surgery and are analyzed by a pathologist. While histopathology provides a basis for prognosis and further treatment of disease, it also remains the "gold standard" for validating new imaging modalities. Beyond the conventional standard, however, whole-mount histopathology provides numerous advantages over selective, small-slide scanning. Huron Digital Pathology offers a whole slide scanning solution for breast cancer research with greater clarity, efficiency, and versatility in the TissueScope™ scanner.

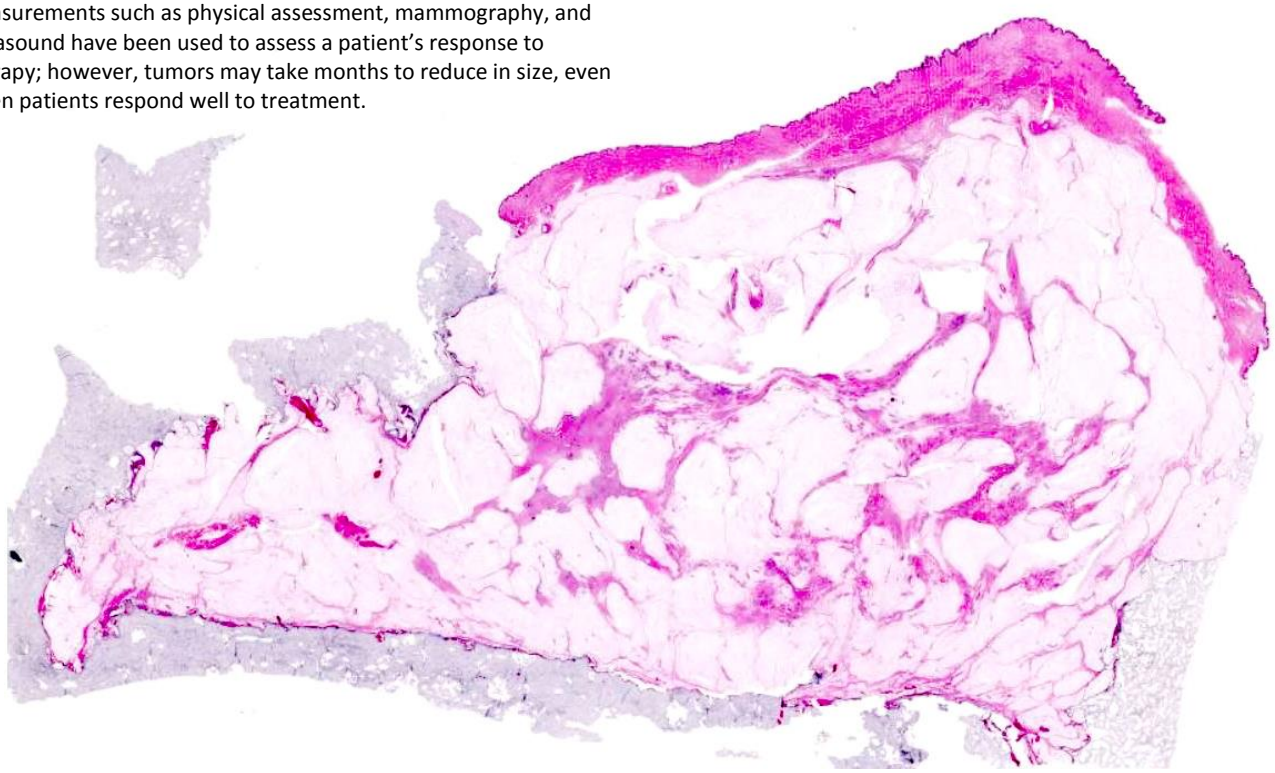

Figure 1. Image of whole-mount breast cancer specimen

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TissueScope - Huron Digital Pathology's Whole-Mount Imaging Solution

In the past, small-format microscopy has forced pathologists to examine small, isolated samples of breast tissue. Breast specimens are relatively large, commonly measuring up to 11" x 11" x 3". When samples of 0.8" x 1.2" x .2" have to be selected, the pathologist's task – determining the extent of the tumor – becomes more difficult. While the pathologist attempts to describe the tumor's extent in 3D, as a whole, only a small representation of 2D images are available. Therefore the specimen may be undersampled, and the extent of the tumor underestimated. When pathologists use small-format histopathology, they can only provide classification-level, feature based inferences between histopathologic findings and radiographic signs. Conversely, the Huron Digital Pathology's TissueScope™ allows for imaging of large-area slides up to 5" x 7" cm, enabling whole mastectomies to be scanned. Whole-Mount histopathology using the TissueScope results in more accurate tumor measurements, capturing areas missed in conventional assessment. In Canada, Sweden, Italy, and the United States, breast cancer researchers are already taking advantage of the superior visual information in large-format histology enabled by the TissueScope.

Secondly, the whole-mount imaging enabled by the TissueScope provides an advantage to researchers because of how it correlates with in vivo imaging. With traditional microscopy, not only would pathologists have to reconstruct their understanding of the breast from small samples, but additionally, because breast tissue is high in fat, it deforms easily after excision, further obscuring its shape. As techniques such as MRI, DOS, Ultrasound elastography, and quantitative ultrasound image the entire breast in vivo, whole-mount histopathology provides them with a better frame of reference. Looking forward, researchers are using the TissueScope to develop 3D images of whole specimens from individual slides, providing a more fully integrated understanding of breast tissue.

Overall, the Huron Digital Pathology's TissueScope provides researchers with an opportunity to more effectively validate new imaging modalities. With up to 0.25µm/pixel resolution at 40x magnification, it provides the sharp, clear image quality necessary to detect heterogeneity in tumors. Because it can scan up to 12 brightfield slides at once in various sizes from 1" x 3" to 6" x 8", and image whole slides in minutes, it provides unmatched versatility and efficiency. With HuronViewer™ and TissueView™ software, images can easily be viewed and managed. Finally, pairing with the TissueSnap™ allows for enhanced workflow optimization.

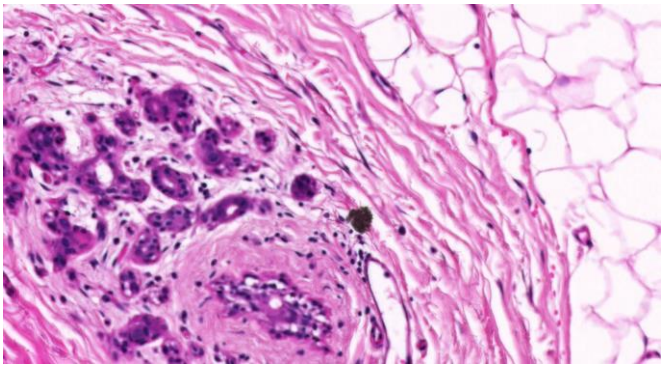

Figure 2. 20X magnification of breast tissue specimen with 0.5µm resolution

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