Image Analysis in Surgical Pathology

Mark C. Lloyd, PhD[a,b,*], James P. Monaco, PhD[c], Marilyn M. Bui, MD, PhD[d,*]

KEYWORDS

• Image analysis • Surgical pathology • Digital pathology

ABSTRACT

Digitization of glass slides of surgical pathology samples facilitates a number of value-added capabilities beyond what a pathologist could previously do with a microscope. Image analysis is one of the most fundamental opportunities to leverage the advantages that digital pathology provides. The ability to quantify aspects of a digital image is an extraordinary opportunity to collect data with exquisite accuracy and reliability. In this review, we describe the history of image analysis in pathology and the present state of technology processes as well as examples of research and clinical use.

OVERVIEW

Image analysis is a method by which meaningful information is extracted from a digital image.[1] By its very nature, image analysis is a reproducible and objective way to quantify a specific aspect of some feature that exists in a sample. This could be the intensity of a staining pattern or the size of a nucleus. In fact, it can be far more complex.

Image analysis is a general term that is not specific to digital pathology. In fact, digital pathology is one of the most recent major medical applications for a concept incepted since the 1940s and 1950s when computer usages in medicine first began to emerge. The growth of image analysis has been considerable in the past 3 to 4 decades as computers have become far more accessible and file storage continues to get less expensive.[2] Well over 100,000 published peer-reviewed articles address medical image analysis (**Fig. 1**). It is clear that in the 1980s image analysis was becoming more accessible. This was due in large part to the expansion of image analysis into radiology. Over the course of the past 2 decades, a new family of image analysis tools has clearly emerged for pathology.[3] In this review, we focus on the emergence of image analysis for surgical or anatomic pathology.

In 1997, a comprehensive review was published by Meijer and colleagues[4] that describes the 3 most general and inclusive areas of image analysis, including (1) morphometry, the measure of geometric features; (2) quantification/counting, the measure of the number of objects; and (3) cytometry/pattern recognition, the measure of cellular features (ie, chromatin). Since the late 1990s, a considerable amount of literature has focused on digital pathology image analysis, and a number of commercial products have become available.

Image analysis was first performed in pathology using cameras mounted in the light path of a standard clinical or research-grade microscope. However, today, high-throughput slide scanning instruments are available. Slide scanners made a considerable mark on the history of image analysis of histologic samples. Slide scanning brought technical and accessibility advantages to the field. By controlling and calibrating the light sources and flattening the background, these instruments produce relatively homogeneous images. Furthermore, by producing whole slide images (WSIs), the pathologist is no longer limited to specific fields of view. Finally, the increasing speed of acquisition of these instruments is bringing a digital pathology workflow to those institutions that are the earliest adopters. In summary, slide scanning technology has facilitated the enhanced the utility of image analysis for pathology considerably. Although some technical, regulatory, societal, and other

[a] Analytic Microscopy Core, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [b] Department of Biological Sciences, University of Chicago Illinois, 845 West Taylor Street, Chicago, IL 60607, USA; [c] Inspirata, Inc. Tampa, FL, USA; [d] Analytic Microscopy Core, Department of Anatomic Pathology, H. Lee Moffitt Cancer Center and Research Institute, 12902 Magnolia Drive, Tampa, FL 33612, USA

* Corresponding author. H. Lee Moffitt Cancer Center and Research Institute, 12902 Magnolia Drive, SRB-4, Tampa, FL 33612.

E-mail addresses: mlloyd8@uic.edu; marilyn.bui@moffitt.org

Surgical Pathology 9 (2016) 329–337

http://dx.doi.org/10.1016/j.path.2016.02.001

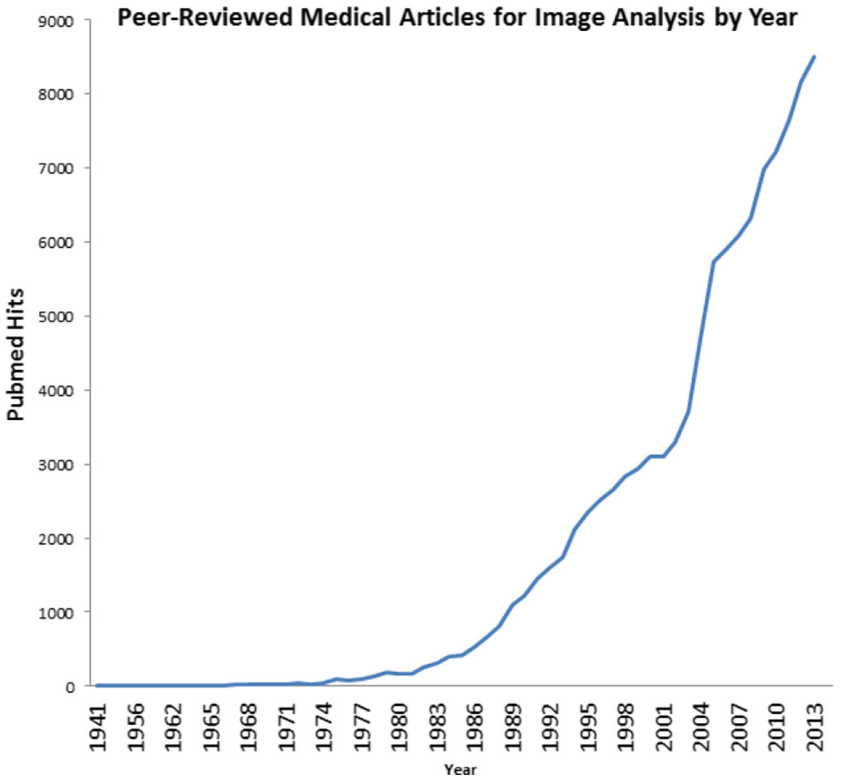

Fig. 1. Peer-reviewed articles available on www.pubmed.gov by year for the search term "image analysis."

challenges remain, the future is bright for image analysis of surgical pathology specimens.

PROCESSES

The routine surgical pathology specimens that are subject to microscopic examination are glass slides with a surface 3 to 4 micro-slices of formalin-fixed and paraffin-embedded tissue sections with various stains including hematoxylin-eosin stain (H&E), immunohistochemical-based stain (IHC), and special chemical stains. Fluorescence-based stain is less frequently used for clinical specimens but common for research specimens. The process of analyzing an image for surgical pathology specimens begins after the image is acquired. The images include the whole slide, portion of the slide, or static images of specific areas of interest. Image acquisition alone does not include image management, image query, or image sharing or related digital pathology subjects. This can, at times, be confusing because commercially available tools often provide a complete digital pathology workflow solution. Image acquisition to archive quality images is the single most important step toward achieving meaningful image analysis result. Issues related to image acquisition will be discussed elsewhere in this issue. For the purposes of this review, we divided the image analysis section into 3 main categories after image acquisition: (1) segmentation, (2) classification, and (3) results. Within each of these 3 categories we address morphometry, counting, and color/texture. This is a massive oversimplification of the utility of image analysis for pathology; however, the goal is to describe in enough detail, for a broad audience, how image analysis can work using surgical pathology specimens.

IMAGE SEGMENTATION

Segmentation is a method for dividing an image into smaller subsegments. By segmenting an image, one can break the image into similar pieces that can then be evaluated in a more meaningful way (**Fig. 2**). Segmentation can be completed using a number of different methods. It is not our goal to describe the advantages or disadvantages of any particular method, or even to create a comprehensive list of methods. Our goal is to describe, in general terms, the depth and breadth of opportunities to parse an image into smaller pieces using the methodology most likely to yield the desired results. For example, well over a dozen families of image segmentation methodologies exist for pathology images. Given the multitude of different techniques, we have chosen a subset