ASI's special spotlight on Veterinary and Digital Pathology with Dr. Aleksandra Żuraw

May 15, 2019

WHAT IS VETERINARY PATHOLOGY?

Veterinary pathology is a pathology specialty performed by veterinary doctors. Like human pathology it can be divided into clinical pathology and anatomical pathology. Clinical pathology uses body fluids like blood and urine and various laboratory tests to diagnose diseases whereas anatomical pathology is based on tissue observed under the microscope or on the computer screen in case of digitalized tissue slides. In anatomic veterinary pathology there are three main areas:

1. **Disease diagnosis** for companion, livestock and zoo animals. This includes biopsies to determine the ongoing disease, and necropsies in order to determine the cause of death. Disease diagnosis can be performed for the

   a. **Private sector** - e.g. companion or sport animal owners, who need to diagnose their animals' disease for treatment or breeding.

   b. **Public health sector** - where it serves the purpose of improving human health by e.g. improving the agriculture and addressing and preventing zoonotic diseases like rabies and food-borne diseases. In the USA veterinary pathologists in this sector work for such government regulatory agencies as the Food and Drug Administration, US Department of Agriculture, Centers for Disease Control and Prevention, and Environmental Protection Agency.

2. **Drug development support** which includes toxicological pathology. In the development of every drug approved for human treatment, there is a pre-clinical and a clinical phase. During the pre-clinical phase the drugs are being tested on animals and during the clinical phase, on people. Veterinary pathologists are crucial to the pre-clinical phase of drug development, where they evaluate the tissue of laboratory animals in pharmaceutical studies for signs of toxicity caused by the drugs the animal were given; 99% of the drug candidates from pre-clinical studies never make it to the clinical phase. The job of a veterinary pathologist is to identify the safe 1% which can be taken further.

3. **Research,** which can be performed in academic institutions, government organizations like the National Institute of Health as well as in pharmaceutical, biotech and chemical companies.

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VETERINARY VS HUMAN PATHOLOGY:

Veterinary pathology is in fact very similar to human pathology with common investigational methods. The microscope is front and center in our work as well. As with human tissues, animal tissues are stained with Hematoxylin and Eosin (H&E) which is the most utilized stain for disease diagnosis and screening. Most cases are resolved based on the H&E stain, see Figure 1. If further investigation is required, more specific methods can be used such as chemical special stains or immunohistochemistry (IHC), see Figure 2.

In addition to diagnosing the disease, pathologists need to quantify its extent or severity. Under the microscope it is usually done in a semi-quantitative way and the process is graded as minimal, mild, moderate or severe. In case of evaluating IHC stains under the microscope, semi-quantitative scorings can be implemented which intend to quantify the intensity and number of stained cells on an arbitrary scale e.g. from 0 to 4 where 0 corresponds to absence of staining and 4 means that many cells in the tissue stain have high intensity.

Figure 1

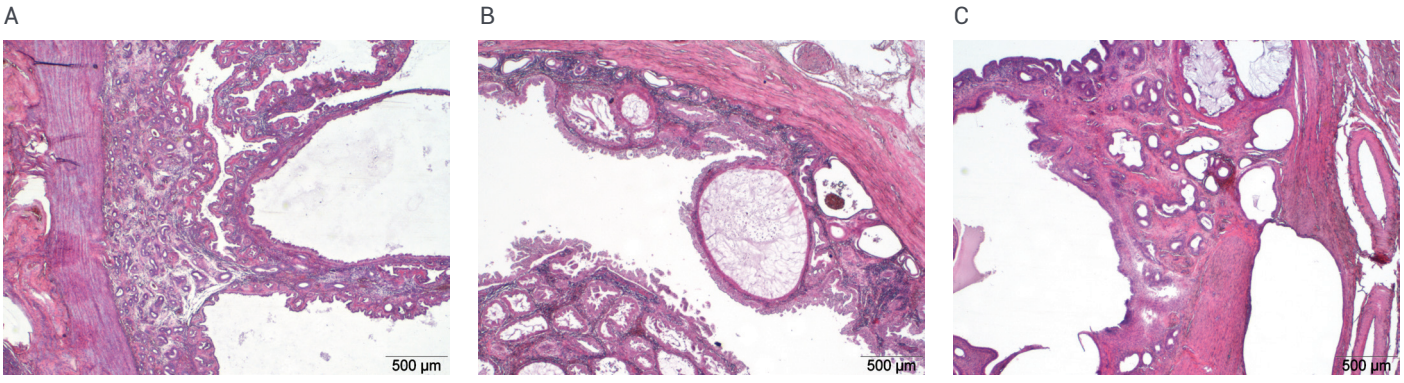

Figure 1: Dog, uterus, mild (A), moderate (B) and severe (C) cystic endometrial hyperplasia. Such a semi-quantitative way of describing pathological lesions is subjective. Adequate computer algorithms enable the objective quantification of tissue changes. For this research project, the correlation of cystic endometrial hyperplasia severity with clinical parameters, such as hormone levels was calculated. The project would enormously benefit from quantifying the changes using image analysis tools (e.g. calculation of the density and mean diameter of the cystic uterine glands) instead of just describing them as mild, moderate or severe.

MINIMIZING SUBJECTIVITY:

Analysis results may vary between pathologists. Even the same pathologist can produce different results depending on the time of the day or the level of stress. The same can be true for histology technicians who develop different staining protocols. The characteristics of a staining may vary from batch to batch and from person to person.To minimize the subjectivity and reduce the error rate, implementation of digital pathology is imperative.The information contained in tissue, like the number of positive cells in IHC can be quantified with computer algorithms if the slides are digitized, which significantly reduces the inter- and intrapersonal variability of semi-quantitative scoring. Analyzing the pathology images with standardized algorithms can make the discipline of pathology more objective and potentially increase the diagnostic accuracy.

Figure 2

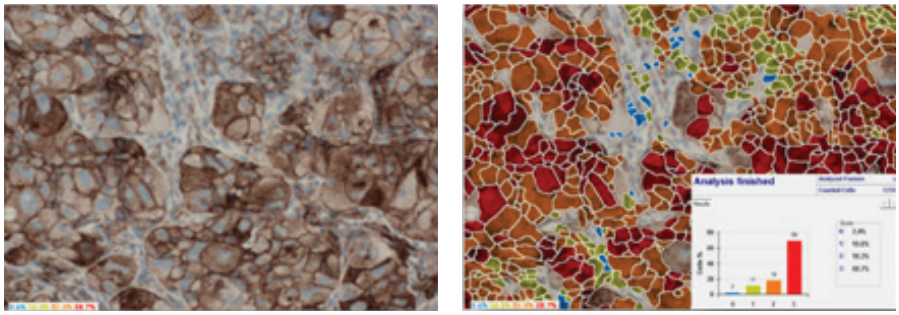

Figure 2: IHC slide, before and after analysis. ASI provides automatic cell classification with statistical analysis on thousands of cells. ASI provides a unique Brightfield imaging & analysis system for a variety of histopathology needs, including quantitative IHC Scoring and Whole Slide Imaging of H&E/IHC samples. Through precise computer-assisted analysis and high image quality, ASI software provides scientific results which can be validated by multiple users. The rich system encompasses digital scanning, imaging, analysis, sharing and reporting capabilities.

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TOWARDS RELIABLE RESULTS:

The main strength of image analysis algorithms for tissue quantification is, that it allows to move away from subjective analysis. Automatic quantification across numerous regions of interest, encompassing hundreds of thousands of cells (rather than limited to a hundred or less counted under the microscope) can be a huge advantage to pathology. Greater statistical analysis provides greater confidence in analysis. As long as the results are accurate and reproducible, image analysis algorithms are a viable tool for pathologists in research settings. In order to use the algorithm results for diagnosis and patient related decisions, they need to be reviewed and approved by the FDA according to the medical device regulations.

ABOUT DR. ALEKSANDRA ŻURAW'S BLOG: DIGITALPATHOLOGYCONSULTING.COM

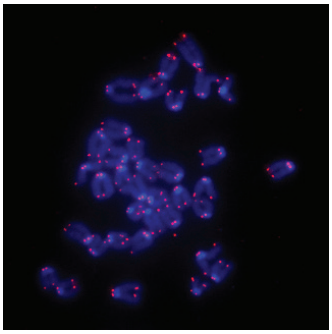
The reason I started the blog was to connect pathologists and computer scientists in order to promote and improve digital pathology. In this discipline, the two professions need to work closely together, especially in the development of image analysis algorithms. Digital image analysis can be a game changer in quantitative digital pathology, but the key here is accuracy. I can't emphasize enough how important it is for the digital algorithm to quantify the relevant aspect of the tissue. While we need to heed new technology, we can't compromise on accuracy. Accuracy supersedes all for the sake of quality health care for animals and humans. If algorithms do not achieve the necessary concordance with our manual evaluation or clinical outcome data we may be increasing speed but not providing any value. For more on Dr. Aleksandra Żuraw, please visit her blog. www.digitalpathologyconsulting.com

ABOUT APPLIED SPECTRAL IMAGING (ASI)
COMPLETE BIOMEDICAL IMAGING AND DIGITAL ANALYSIS SOLUTIONS FOR LABORATORIES AND HOSPITALS:

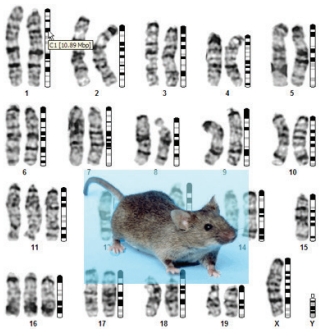
ASI's advanced microscopy solutions for genetic and oncological diseases apply to research and veterinary laboratories as well. With the HiBand solution, you can create your own karyotyping table for any specie, and teach the system how to karyotype G-banded slides based on a few metaphases towards faster and optimal analysis. This unique algorithm is calibrated by an ASI expert during the installation process. The company's HiSKY solution, where karyotyping is based on spectral analysis, for the automatic identification of translocations and chromosomal origins, for multi species is limited to only mouse and rat.

For more information on ASI's full range of products, please visit the company's website at www.spectral-imaging.com or reach out for a live demo on any application.

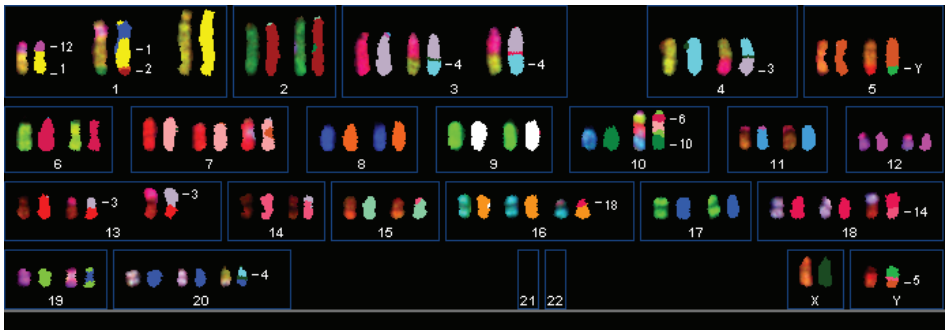
Mouse metaphase



Telomeric analysis



Chromosome analysis and karyotyping



Spectral imaging - rat