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Assisting Pathologists in Detecting Cancer with Deep Learning

Friday, March 03, 2017

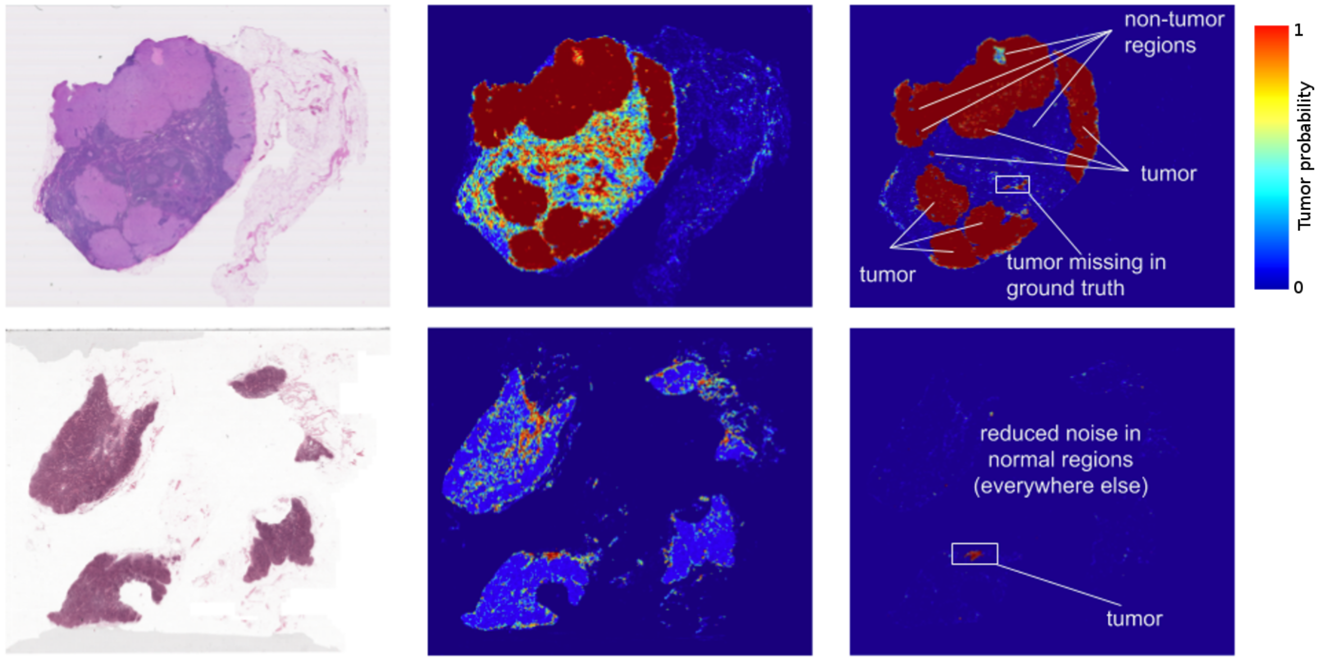
Posted by Martin Stumpe, Technical Lead, and Lily Peng, Product Manager

A pathologist's report after reviewing a patient's biological tissue samples is often the gold standard in the diagnosis of many diseases. For cancer in particular, a pathologist's diagnosis has a profound impact on a patient's therapy. The reviewing of pathology slides is a very complex task, requiring years of training to gain the expertise and experience to do well.

Even with this extensive training, there can be substantial variability in the diagnoses given by different pathologists for the same patient, which can lead to misdiagnoses. For example, agreement in diagnosis for some forms of breast cancer can be as low as 48%, and similarly low for prostate cancer. The lack of agreement is not surprising given the massive amount of information that must be reviewed in order to make an accurate diagnosis. Pathologists are responsible for reviewing all the biological tissues visible on a slide. However, there can be many slides per patient, each of which is 10+ gigapixels when digitized at 40X magnification. Imagine having to go through a thousand 10 megapixel (MP) photos, and having to be responsible for every pixel. Needless to say, this is a lot of data to cover, and often time is limited.

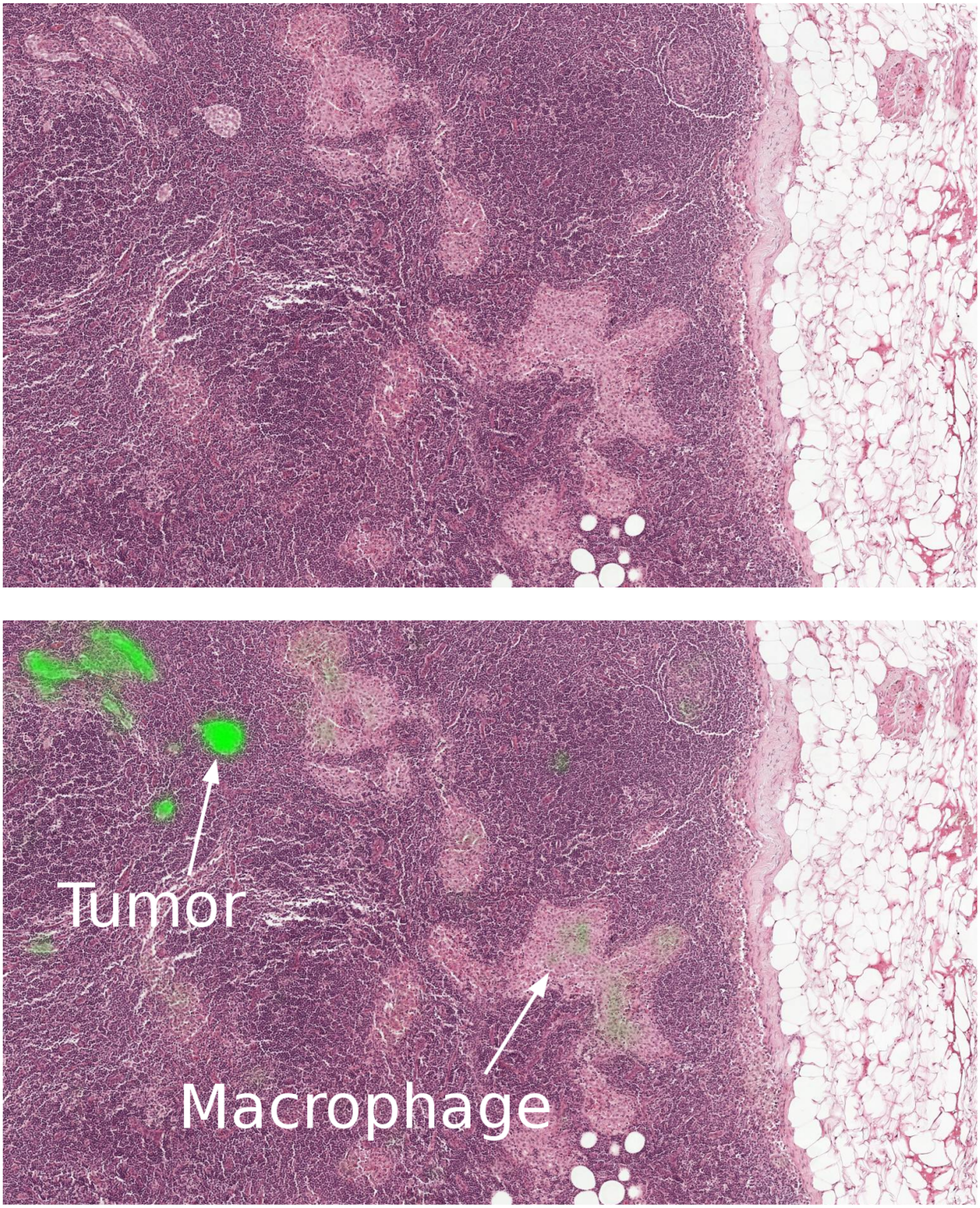
To address these issues of limited time and diagnostic variability, we are investigating how deep learning can be applied to digital pathology, by creating an automated detection algorithm that can naturally complement pathologists' workflow. We used images (graciously provided by the Radboud University Medical Center) which have also been used for the 2016 ISBI Camelyon Challenge[1] to train algorithms that were optimized for localization of breast cancer that has spread (metastasized) to lymph nodes adjacent to the breast.

The results? Standard "off-the-shelf" deep learning approaches like Inception (aka GoogLeNet) worked reasonably well for both tasks, although the tumor probability prediction heatmaps produced were a bit noisy. After additional customization, including training networks to examine the image at different magnifications (much like what a pathologist does), we showed that it was possible to train a model that either matched or exceeded the performance of a pathologist who had unlimited time to examine the slides.



Left: Images from two lymph node biopsies. **Middle:** earlier results of our deep learning tumor detection. **Right:** our current results. Notice the visibly reduced noise (potential false positives) between the two versions.

In fact, the prediction heatmaps produced by the algorithm had improved so much that the localization score (FROC) for the algorithm reached 89%, which significantly exceeded the score of 73% for a pathologist with no time constraint[2]. We were not the only ones to see promising results, as other groups were getting scores as high as 81% with the same dataset. Even more exciting for us was that our model generalized very well, even to images that were acquired from a different hospital using different scanners. For full details, see our paper "Detecting Cancer Metastases on Gigapixel Pathology Images".



A closeup of a lymph node biopsy. The tissue contains a breast cancer metastasis as well as macrophages, which look similar to tumor but are benign normal tissue. Our algorithm successfully identifies the tumor region (bright green) and is not confused by the macrophages.

While these results are promising, there are a few important caveats to consider.

- Like most metrics, the FROC localization score is not perfect. Here, the FROC score is defined as the sensitivity (percentage of tumors detected) at a few pre-defined average false positives per slide. It is pretty rare for a pathologist to make a false positive call (mistaking normal cells as tumor). For example, the score of 73% mentioned above corresponds to a 73% sensitivity and zero false positives. By contrast, our algorithm's sensitivity rises when more false positives are allowed. At 8 false positives per slide, our algorithms had a sensitivity of 92%.
- These algorithms perform well for the tasks for which they are trained, but lack the breadth of knowledge and experience of human pathologists — for example, being able to detect other abnormalities that the model has not been explicitly trained to classify (e.g. inflammatory process, autoimmune disease, or other types of cancer).
- To ensure the best clinical outcome for patients, these algorithms need to be incorporated in a way that complements the pathologist's workflow. We envision that algorithm such as ours could improve the efficiency and consistency of pathologists. For example, pathologists could reduce their false negative rates (percentage of undetected tumors) by reviewing the top ranked predicted tumor regions including up to 8 false positive regions per slide. As another example, these algorithms could enable pathologists to easily and accurately measure tumor size, a factor that is associated with prognosis.

Training models is just the first of many steps in translating interesting research to a real product. From clinical validation to regulatory approval, much of the journey from "bench to bedside" still lies ahead — but we are off to a very promising start, and we hope by sharing our work, we will be able to accelerate progress in this space.

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1 For those who might be interested, the Camelyon17 challenge, which builds upon the 2016 challenge, is currently underway.↩

2 The pathologist ended up spending 30 hours on this task on 130 slides.↩

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Jeff Dean via Google+ 3 months ago (edited) - Shared publicly

I'm very excited about the work our group (g.co/brain) is doing in various areas of medical imaging. Today, we published a preprint of a paper titled *"Detecting Cancer Metastases on Gigapixel Pathology Images"* by Yun Liu, Krishna Gadepalli, Mohammad Norouzi, George E. Dahl, Timo Kohlberger, Aleksey Boyko, Subhashini Venugopalan, Aleksei Timofeev, Philip Q. Nelson, Greg Corrado, Jason D. Hipp, Lily Peng, and Martin C. Stumpe.

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3 months ago (edited)
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James Salsman 3 months ago (edited)
+**Jeff Dean** cmusphinx volunteers this +**Google Summer of Code** are going to model a vocal tract: cmusphinx.sourceforge.net - Project Ideas [CMUSphinx Wiki]
Would you please co-mentor that? I'm not sure whether Kevin the Phoria guy is available.

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A pathologist's report after reviewing a patient's biological tissue samples is often the gold standard in the diagnosis of many diseases. The reviewing of pathology slides is a very complex task, requiring years of training to gain the expertise and experience to do well. Even with this extensive training, there can be substantial variability in the diagnoses given by different pathologists for the same patient, which can lead to misdiagnoses.

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subhashini venugopalan 3 months ago
+**Armada jakenson** ah I guess you are referring to tissue samples. I think it's a fair question. In reality, based on initial analysis one could request for more tissue samples from the patient to be certain. In the camelyon 16 dataset, each slide is a single sample from one individual. In this experiment one can view both the pathologist and the model

Armada jakenson 3 months ago
+**subhashini venugopalan** The Cure for Cancer has been around since the 1920s or 1930s! There WAS an inventor that invented the cure for cancer around then and when he went to patent it, his labs were burnt down, his invention was dismantled, and the cure suppressed! HOW come that avenue has NOT been brought back and used?

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MicheleElys MER 3 months ago

WOW this has been necessary for a very long time. For many forms still had not been detected Thank you +**Wayne Radinsky**

Wayne Radinsky 3 months ago *+1*

You're welcome, +**MicheleElys MER**.

Macle Johnson 2 weeks ago - Shared publicly

CONTACT MR PAUL Smith call (+2349055346865 or WhatsApp him +2349055346865 or email:
illuminatiworldofsociety1@gmail.com
Hello everyone I am mr Charles Adamson from Liberia, I am giving a testimony on how I joined the illuminati brotherhood, I was trying to join this organization for so many years

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Dr. Shaunak Das 1 month ago - Shared publicly

This is awesome. Thanks to Google for this groundbreaking technology.

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Very excited about the work we're doing in healthcare to help doctors analyze data faster and more reliably.

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Brandon Ballinger 3 months ago
Woo! Congratulations.

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+5 1

Ilya Shmulevich 3 months ago - Shared publicly
Great work and congratulations on such an impressive achievement!
I want to let everyone know that radiology images from The Cancer Imaging Archive (TCIA) (>1.4 million radiology image files) as well as the pathology and diagnostic images previously available from the Cancer Digital Slide Archive (CDSA) (>30,000 tissue slide images) are all now available in the ISB-CGC (isb-cgc.org) open-access Google Cloud

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Jeff Dean on this very interesting work with a link to the paper in his post.

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Clarisse Nigaud 3 months ago

Interesting indeed!

Raad Alshahry 3 months ago - Shared publicly

Very interesting and promising. I'm doing my master's degree in HPC and Deep Learning and I've got a child with cancer. I'm interested to be involved if possible.

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Data Scientist Mike Tamir 2 months ago - Shared publicly

Assisting Pathologists in Detecting Cancer with **#AI #DeepLearning #MachineLearning #DataScience**

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Just stick with it, and keep working on it. Don't orphan it or abandon it. Keep it going, make it a "thing".

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