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Utrecht digital workflow

Prof van Diest: Good afternoon. It's a pleasure for me today to tell you about the UMC Utrecht digital workflow in pathology. I'm very grateful for the invitation to share this with you. Now, there's a lot of advantage to digital pathology. The first ones are listed on this slide, and there's a lot more on the second slide. I'm not going to go over all of them. They will become a bit clearer during this presentation, but I think at least it makes clear that there's many of them and many have to do with patient safety and making the workflow of pathology more efficient. So, this is the workflow that we currently have in UMC Utrecht. Our setup is based on the SECTRA pathology PACS, which is hosted on a VNX image data server, to which all the different components of the system are connected. We have four high-speed scanners and one special scanner for fluorescence and big slides. And also, all the other modalities that produce images in the department... the images are being stored on the VNX image data server. And we direct everything from the PACS. Now, this is interfaced with the storage. There is interface with AI, which I will disclose a bit later. And we are interfacing with radiology as well and the pathology reporting system, which is at present Delphic AP. So, with regard to the implementation process, there's a number of things that we came across, which have to do with hardware, software, a few lab issues and also, change management. So, this is a scanner room. We have, as I said, four of these big scanners, one dedicated to research for which we have quite a bit of business, and together they scan about 1500 slides a day. And the average size of the slides is about one gigabyte per slide. So, that's quite an amount of data. The protocols for scanning are fully automated and the scanners are being operated by one or two technicians, depending on the time of the day. Usually, in the morning, we have about two to take care of all the different slides that need to be scanned that come out of the lab. And on the right-hand side, you see here, the big screen by which the technicians direct the different scanners. And there is this one smaller scanner, which is for priority cases, but also, for cytology, 3D, fluorescence, big slides. Our scanner room is the nicest room in the department because it's very well with regard to climate. The scanners produce ozone and a lot of heat so, we have very good air conditioning system to the point that the hair of these technicians is almost being sucked into the air conditioning system. For the hardware, we had to switch to a 2D barcode to store all the information that the digital workflow system needs to make sure that everything happens on the right time. The VNX server is hosting the PACS and that's a very double-workflow type server. That means that everything will be up all the time. It's at

present a standalone, but we plan to do an integration with radiology a bit later. Now, the network connections are pretty standard because the streaming is very good. So, one gigabyte connections and switches suffice. The computers have to be up to speed with what we do here with regard to graphics cards, but also, turned out that the CPU speed is very important to make sure that we handle these images with the correct speed. We have standard 4K big screens so, not the very expensive monitors that radiology uses and, in our experience, these suffice. Of course, the desk looks a little bit different. So, most of us have three to four screens, as you see here, display all the different software programs. And this is the gizmo that we use to direct the PACS, a 3D mouse that works very well in our setup. The storage is a big deal if you keep all the images as we do. The first six years, we scanned at 20x, and from 2015 onwards, we scanned at 40x, and it's a hard disk-based system of isilon. And it's, at present, it's two petabytes of data. And we plan to store everything permanent because we think that's a true asset of having a digital workflow. This is, to a large extent, it's DICOM image format-based. And some people consider it to be expensive. We think it's worth the money to have all these images just available one click away. The connections. This is not to go over everything in detail, just to impress you and to show you that this is a big deal. And you have to think beforehand and very well about the setup, about the architecture of your system, to make sure that everything kicks in at the right time and the information it's available when it's needed during the scanning and the rest of the workflow. And this is a true asset. SECTRA is a company that is watching all its clients all over the world. And as soon as something goes down somewhere in our system, SECTRA will pick it up in this war room, as I tend to call it, in Linkoping in Sweden, and correct it before we even notice that we have a problem. So, that's very good. And this way, they can guarantee us an uptime of more than 99%. The software is a very user-friendly, very intuitive, with different components. For us, the PACS is leading in a workflow with lots of folders that you can configure yourself. And then these folders start different cases. So, this is my own work folder with a few cases here. If you click on a certain case, all the prior cases open up and all the prior images of these prior submissions are available just one click away. At the bottom, the thumbnail images that give you a good idea of how big the case is. And on the right, you see the screen where we view the images with the thumbnails here at the bottom, where you can just click from one slide to one image to the next very quickly. The request form is here on the top-right. So, annotations and measurements are very easy to make like this. And we do this all the time they're being stored. And it's a very nice tool to make the microscopy and your conclusion in the end. Also, for more complex cases like prostate biopsies, where you have to do a lot of measurements, this is a very easy way to make all these measurements. Slides can be viewed side by side, with four slides at the same time. They're being synchronized so, if you zoom into the one, also, the other ones will zoom in and out at the very same time. So, that's a true asset if you want to do multiple things on one screen. We have tracking in the system. That means that everywhere we go in the images, the system tracks where we are. The more yellow with this, the higher magnification we have for view this particular part of the image. So, that really helps us to make sure that we have seen everything which is available on the slide. This is the chat function, it's available and we use it all the time to consult one another. You can really chat like, you know, this particular image, you can send the link. "What do you think?" And you get an answer usually quite directly, and that's a very convenient way to consult your colleagues internally, or even externally. With mitoses counting tool, where you can select an area, mark the different mitoses that you see, and the image will register where you have been. And at the end, it will produce this microscope that says you have found 10 images in 1.4 square millimeters. So, that makes it look easier to remember if it's were seven images, seven mitoses in eight images, or was it eight in mitoses in seven images. So, that's a very convenient tool that helps us. This is an AI-based Ki67 counting tool that works quite nicely. So, you draw a freehand area or you start a circle, and the system will recognize the brown cells and give you, in this particular case, that 10% of the cells are positive. There are a few lab issues that you have to consider. We switched to three-micron thick sections because the standard four-micron was producing not very good images. And that helped a lot to get a better image, especially, of the nuclei. The mounting has to be central because otherwise the scanners will not pick it up and it will be on the outside of the images. You have to do restrictive mounting, not so many ribbons on one slide, because it will take more time to scan them and more

time to fuel them. Also, the lab has to make sure that there are no glue remnants on the slides, because if that is the case, then, the slides will stick to one another in the racks that go into the scanner. The slides need to dry very quickly so that means that we switched back from neoclear to old-fashioned xylene again. For the workflow, we had to develop different scanning protocols because the scanners that we use from Hamamatsu are not just turnkey, but everything can be tuned to special cases like special stains, immunohistochemistry, fatty slides, big slides and fluorescence. Slides need to be cleansed very well before the scanning, otherwise, the images will not be optimal. And we have automated quality control and rescan. Case assembly and release is automatic based on the information in the barcodes. And when we implemented the system, we had a double workflow with slides and the digital images for about half a year to make sure that everybody got used to working with the system. And of course, the lab management system needs to be inducted in a few ways, like, I want see the slides button, or rescan the slide button. Change management. Switching from the traditional microscopy-based pathology to digital pathology is a big deal. So, it's a change management, here, is something which is very important. So, we explained all the time how and why we did this. We have regular meetings and email updates, and you have to deal with the dinos by, you know, having them convince themselves by showing them the system and giving them a few incentives like, you know, "If you don't want to use the system, you have to go through the archive to find the slides to prepare your multidisciplinary meeting." And that really helped in our hands to convince everybody. Of course, proper training is very important for everybody in the department having to deal with the workflow. And to make sure that everybody was involved in this process, we created all these working groups to make sure that about everybody in the department was part of some working group to make sure that they had control, the had involvement and they could come up with their own solutions. And that worked very well in our heads. We have an integration with radiology and that's very nice. We have a button here in the system that says Extended patient search. And if you click it, you get all the imaging information from the radiology department who also has a SECTRA PACS, and you can click on something and then, the images will pop up, even, as a workaround without the hospital information system. And it also works the other way around. The radiologists have a pathology button in their PACS that they can click. And if they do, they can get to see all the images. And that works very well in our collaboration with our friends from radiology. So, traditional microscopy-based practical sessions with the students, we don't do anymore. We do everything digitally and that works a lot better, what you can see here, is that even the students appreciate it a lot more. The rating for these virtual microscopy practicals went up from 6.6 to 7.9 and from 5.7 to 8.2. So, the students like it a lot better to work with digital images instead of the traditional microscopes. Now, we have ambitious plan for integration of artificial intelligence in our lab. There's a number of tedious irreproducible tasks where we need support to do a better job, to do a more efficient job, to do a more reproducible job. For instance, mitoses counting, assessment of nuclear areas assessment, let's say within the framework of breast cancer grading, tubule formation, finding metastases, quantification of the immune infiltrate in different tumors, tumor versus stroma quantification, immunohistochemical scoring, and perhaps also, in the end, a general morphological diagnosis that progresses with regard to the latter is yet limited. So, this is the ambitious roadmap that we have. We are implementing a number of algorithms as we speak. And the first one is in our system. That's the homemade mitoses counting algorithm that we have to fill up together with the Technical University in Eindhoven. And it's within a system. And I will show you a short movie a little bit later on. We have bought the AI algorithms from Visio Pharm. So, we will be implementing them during the first quarter of next year, or perhaps, if it works for all, even within the last quarter of this year, but time's running out a little bit. So, let's say it's gonna happen next year. ER, PR, HER2 and also lymph node metastases finder, they will come with the new scanners that we bought to replace our current Hamamatsu scanners. We also have a collaboration with the Proscia AI firm. They have a nice algorithm to stratify cases into complicated or easier, to make sure that all our pathologist in the department can help with the easy cases, but the experts, dermatopathologists, can focus on the difficult cases. Also, this algorithm will be implemented during the first quarter of next year. And then, during the remaining quarters of 2022, we'll also implement a lymph node metastases finder that we have made in collaboration with the

University of Radboud in Nijmegen, and also, an AI algorithm for immune infiltrate quantification. And we have another homemade algorithm for melanocytic lesions that we will also try to implement during the course of next year. So, this is a short movie of our homemade algorithm. And what you see here is the SECTRA PACS system, right? I will now activate the algorithm. This is a breast cancer case, and that will give you an idea of where we are with implementation of these algorithms. So, basically, you have to select an area interactively, and this time, so, you right-click this, and you select an area where you would like the mitoses to be counted. And then, we have cut-out a little bit of the movie because then the algorithm starts calculating. And after about a minute, it comes up with these objects, which here on the top left is a gallery with potential mitoses and on the bottom, a few other objects that could be candidates, but are probably not mitoses. By very easily clicking on the symbol here, you will go to the objects. You can review it. You can decide if it's a mitosis or not. If it is, you can stay in the mitosis's gallery, if it's not, you simply drag it to the non-mitoses gallery. And at the end, you will turn up with the final number of mitoses. And I think you can see here that the algorithm has found an interesting number of the nicely looking mitoses. You verify the algorithm and then the output is being saved in the system. So, this is where we are at the end of 2021 with regard to the digital workflow at the UMC Utrecht. We have a fully digital pathology workflow where we have almost everything digitally available, except for cytology, which we expect to do in 2022. Doing digital cytology is more complicated. You have to scan in 3D, which is more scanning time, which is more storage time. So, we have not done that at this very moment. We're waiting for the dedicated cytology Hologic scanner that we hope to get in 2022. We have a sustainable, fully digital archive that dates now back 12 years with lots of data, which is one click away available. And that's a very big asset in our system. And we experience that every day. So, we hope to be able to keep it up like that. And I think we do store more information every year, but after a few years, the storage becomes cheaper. And I think in this way, we have a sustainable, fully digital archive, which is future proof. We have radiology-pathology integration. We store most of our images in DICOM format and we have a good converter for the images, if that would need to be the case in the future. We have a national image exchange platform between the pathology labs in Holland, which I've had no time to discuss. It's called the PIE system. It's a very nice system to do digital revisions and consultations. And we have an ambitious program for integration of AI applications, where we have a made the first steps, and we hope to implement more algorithms during the course of next year. And I've no doubt that these AI algorithms are going to help us to do a quicker and better job and a more reproducible job to make sure that our patients get a better diagnosis than we have right now and get the optimal treatment. So, that's what I had in mind to tell you, I think you very much for your attention.