Scanners for Digital Pathology Turning Tissue into Pixels

Peter Schüffler and Volker Bruns

Digital slide scanners are at the heart of digital pathology, forming a steady beat of slide scans and a constant data flow. While very mature and proven models are available, this technology is still evolving, and the number of new scanning devices with novel features is steadily growing further.

In the past decade, digital slide scanners got significantly faster in digitizing slides. Scanning a hematoxylin eosin (HE)-stained tissue slide can be as quick as 30 seconds, fully automatic without manual interaction, at a high resolution (e. g., 0.5 to $0.25 \,\mu$ m/pixel). This contrasts with older devices that require manual selection of the tissue area, optional correction of focus points, and with a slow scanning time over five or ten minutes. Various models with advanced features are today available, e. g., with high slide capacity, particular robustness to preparation artefacts, with integrated slide archival, with scalability to grow as the demand increases, with a very affordable price, with support of online live AI analysis, models that are remote controllable and support live-streaming, or that are portable like a smartphone.

Big advances have further been achieved for automation, integration, and compatibility. Artificial Intelligence (AI) automatically detects the tissue area on a



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slide and controls image quality during and after the scan. Continuous loading of the scanners without interrupting the scanning process and automatic processing of the loaded racks and slides without manual interaction allows for seamless and easy handling. Workflow compatibility on hardware level, e. g. with the slide racks of the stainer machines, and on software level, e. g. for data exchange with the Laboratory Information System (LIS) or with the digital slide viewing software, promise plug'n-play-like integration of new scanners into the lab.

Current Challenges with Digital Slide Scanners ...

In a daily routine workflow, however, the digitization process still faces a few challenges. Scanner vendors naturally introduced their own image management software, varying in slide storage organization, unique image identifiers, whole slide image data formats and visual appearance of the images. This vendor and model heterogeneity complicates a mixture of scanners in one clinical lab, as they all come with their own software, interfaces, maintenance workflows, and crossdevice compatibilities, increasing the workflow complexity. A single system is easier to administrate and favorable.

However, from a research perspective and for specific requirements and features of individual scanner models (e. g. fluorescence scanning, polarization scanning, cytology, or others), a mixture of scanners would be favorable. The heterogeneity in visual slide representations of different scanners can make AI models more robust and generalizable, if learned during training. Also, downstream software applications, such as clinical and non-clinical AI-models, increase the heterogeneity







in the lab further, might be compatible with only a subset of scanner devices and introduce additional interfaces and viewing software for human interaction.

... and Their Solutions

This gap between simplicity for an efficient lab workflow and complexity due to hardware and software heterogeneity is currently being closed. E. g., an image format towards a digital imaging and communications in medicine (DICOM) standard is being developed and discussed, e. g. by the European bigpicture consortium¹. More and more scanners $\overline{}^{T}$ https://bigpicture.eu

generate DICOM images that can be shared across different systems and viewers. Further, middleware software such as digital pathology solutions fill the gap between LIS, scanners and AI. Such solutions are not necessarily needed but drastically detangle the specific requirements of individual system combinations and configurations providing more freedom and flexibility when interacting in a broader laboratory landscape with multiple vendors.

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COMPANY NAME

Hamamatsu Photonics

Mc	del name	NanoZoomer \$5/10MD	NanoZoomer S20MD
IVIC		Reportion or placed on cart	Reportion
	Width y height y depth (cm)	75 v 64 v 69	//////////////////////////////////////
	Weight (kg)	123 6 (188 6 with cart)	52
	Supported slide dimensions (width x length x thickness in mm)	25-26 x 75-76 x 0.9-1.2	25-26 x 75-76 x 0.9-1.2
	Slide handling	Automated, horizontal	Automated, horizontal
۱data	Lenses (magnification numerical aperture)	20x 0.75	20x 0.75
ysten	Resulting magnification per lens (x-fold)	20x; 40x	20x; 40x
S	Pixel resolution (µm/pixel) per lens	20x: 0.46; 40x: 0.23	20x: 0.46; 40x: 0.23
	Digital image sensor (type pixel MP)	CMOS -	CMOS -
	Image processing	Automatic white balance, auto focus	Automatic white balance, auto focus
	Supported microscopy methods	Brightfield microscopy	Brightfield microscopy
	Light source types	LED	LED
	Slide loader (type loading capacity)	540 slides 30 slide cassettes; 360 slides 20 slide cassettes	20 slides 1 cassette
ta	Supported stainer racks (type)	Sakura 4768 20-slide cassette; Leica Universal 30-slide cassette	Sakura 4768 20-slide cassette; Hamamatsu Slide cassette
ce da	Image formats (incl. conversion)	NanoZoomer Digital Pathology Image (NDPI), DICOM	NanoZoomer Digital Pathology Image (NDPI), DICOM
nan	Z-stacks (number distance)	1–99 layers up to 100 µm	1–99 layers up to 100 µm
erforn	Scanning speed for an area of 15 x 15 mm (enlargement I sec.)	20x; 40x approx. 30 sec (area of 15 mm × 15 mm square with 5 focus points)	
Pe	Throughput: slides/h	≥82	80
	Integrated QC and Indication	Yes, manual QC or integrated focus score, with possibility of automatic rescan at spec levels	
	Viewer	Stand-alone, included with NZAcquireMD software, or optional web-based server managed software for scanning and viewing	
	Al-Support	Yes, intelligence mode tissue detection to detect areas of tissue on the slide macro image	
	Works with Cloud and/or onPrem	Cloud and on-prem storage	Cloud and on-prem storage
ling	Self-calibration	Automatic self-correction	Yes
work	STAT mode, prioritised slides	Yes, prioritise and organise the scanning order of racks or slides.	Yes, although it is not required with a low capaci- ty scanner you can define the order of scanning.
Ne	Barcode scanner (1D, 2D)	Barcode driven workflow with 1D and 2D barcode	support
n and	Image data management	Hamamatsu image formats are compatible with all major providers of image management soft- ware. We can also provide our NZConnect software for management of images.	
ratior	Interface protocols	Supports HL7 interfacing and automated DICOM image distribution to IMS, PACS, and VNA for efficient data exchange	
Integ	Connection to LIS/PIS	HL7 interfacing for LIS and PIS integration, automated LIMS data association via barcode recogni- tion, bidirectional communication with LIS/PIS, NZConnect API for custom LIS/PIS integration.	
	Certifications	Compliant with IVDR, IvDO and UK MDR2002	
	DICOM supported	Yes	Yes
	Embeds color profile	Embedded CCM	Embedded CCM
Software development kit (SDK) available Unique selling points, special features		Yes The NanoZoomer S540MD is a large capaci- ty, high-throughput, automated scanner that seamlessly integrates to lab environments. With Sakura cassettes support, touchscreen inter- face it is intuitive requiring minimal user input.	Yes The NanoZoomer S20MD is a high-speed, com- pact, and adaptable scanner that adds flexibility and scalability to your digital pathology workflow. It supports Sakura cassettes and automatic scanning for minimal user input.

Abbreviations: CCM = Color Correction Matrix, DX = Diagnostics; LS = Lense System; RX = Research; WD = Working Distance

Roche Diagnostics Deutschland GmbH		Sysmex Deutschland GmbH 3DHISTECH LTD
Ventana DP600	Ventana DP200	Pannoramic 480 2 nd Gen.
Integrated, compact benchtop device	Integrated, compact benchtop device	Integrated, benchtop
74 x 74 x 67	50 x 68 x 46	119 x 100 x 90
75 + 11 (Touchscreen Monitor + PC)	46,5 + 11 (Touchscreen Monitor + PC)	240
25–26 x 75–76.5 x 0.9–1.4	Single: 25–26 x 75–76.5 x 0.9–1.4 Double: 51–52 x 75–76.5 x 0.9–1.4	Single: 25–26 x 75–76 x 0.9–1.2 Double: 50–51 x 75–76 x 0.9–1.2
Horizontal, slide remains in the tray (exclusion of	glass breakage)	Automated, horizontal
20x 0.75 (Nikon ApoChromat, WD = 1.0 mm, add	ditional LS for 40x)	20x 0.8; 40x 0.95; 40x 1.2 (water immersion)
20x; 40x	20x; 40x	Up to 57x; 113 x; 113x (depending on camera type)
20x: 0.46; 40x: 0.25	20x: 0.46; 40x: 0.25	0.18; 0.09 (depending on camera type)
CMOS Tri-Linear 24	CMOS Tri-Linear 24	CMOS 12; 21; 25 (depending on configuration)
Automatic white balance, ICC color profiles, dyna	mic autofocus, AI-supported tissue recognition	Automatic white balance, auto focus, color calibrated
Brightfield microscopy	Brightfield microscopy	Brightfield microscopy, polarization (optional)
LED	LED	Pulsed xenon lightsource
Slide tray 40 trays with 6 slides each (240 in total)	Slide tray 1 tray with 6 slides	Racks up to 480 slides
-	-	Sakura, Leica
BIF, TIF, DICOM	BIF, TIF, DICOM	Native: MRXS, DICOM, export to svs or tiff
15 0.5–1.5 μm		30 0.2–10 µm
20x 36 sec; 40x 73 sec		40x approx. 30 sec
20x: approx. 70 (time to view); 40x: approx. 40 (time to view)		80
Yes, manual or automatic advanced image quality check	Yes, manual image quality check	Internal QC for focus quality
Slide Viewer (stand-alone), navify Digital Patholog	gy IMS (web-based)	Stand-alone and web-based
Yes, with navify Digital Pathology IMS		Yes, Al supported tissue detection
Slide Viewer (on-prem), navify Digital Pathology II	MS (cloud)	On premise
Yes	Yes	Yes
Yes, trays can be prioritized	-	Yes
1D, 2D: DATAMATRIX, PDF417, QR code	1D, 2D: DATAMATRIX, PDF417, QR code	1D, 2D
IVD-compliant IMS for diagnostics (also across lo	cations): navify Digital Pathology	RX: SlideCenter; DX: CaseManager
HL7, DICOM	HL7, DICOM	HL7
Yes	Yes	Yes
CE-IVD, FDA	CE-IVD, FDA	DX: IVDR
Yes	Yes	Yes
ICC color profiles	ICC color profiles	Yes
On request	On request	Yes, 3DHistech SimpleSlideInterface
Medium to high throughput in histopathologi- cal routine diagnostics, CE-IVD system, can be combined with the IMS navify Digital Pathology and thus access to a variety of algorithms is possible	Scanning of double-width slides is possible, ideal for frozen section application, CE-IVD system, suitable for cytology and histopathology, combi- nable with the IMS navify Digital Pathology and thus access to a variety of algorithms is possible	With all-in-one Server PC with up to 40 GB storage, only high-troughput scanner with 40x objective, water immersion or polarization mode, RX package includes IMS (SlideCenter) and quantification software, DX package includes IMS (case manager), viewer and diagnostic applications AI and monitoring software