An Update in Pathology for Solid Organ Transplantation

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2nd Annual UNMC Transplant Symposium

Saturday March 22, 2025, 10:30a

Conflicts of Interest

- I have no relevant conflicts of interest to declare.

Pathology Needs in Transplant

- 14,000 deceased organ donors are available on average per year
  - Each of these individuals provides an average of 3.5 organs
- 6,000 living donor organs per year
- Pre-transplant assessment is often conducted on donors / recipients
  - Often assessed by general anatomic pathologists
  - Discrepant interpretations may adversely impact organ acceptance
- Post-transplant biopsies may be conducted if rejection is suspected

Distribution of Expertise

- Digitization of tissue slides may enable exposure of difficult or marginal biopsies to be assessed by on-call ‘experts’ to better enable access

> J Pathol Inform. 2021 Nov 1:12:41. doi: 10.4103/jpi.jpi_23_21. eCollection 2021.

Advantages of Using a Web-based Digital Platform for Kidney Preimplantation Biopsies

Flavia Neri [1], Albino Eccher [2], Paolo Rigotti [1], Ilaria Girolami [3], Gianluigi Zaza [4], Giovanni Gambaro [4], MariaGaia Mastrosimini [2], Giulia Bencini [1], Caterina Di Bella [1], Claudia Mescoli [5], Luigino Boschiero [6], Stefano Marletta [2], Paolo Angelo Dei Tos [5], Lucrezia Furian [1]

Affiliations + expand

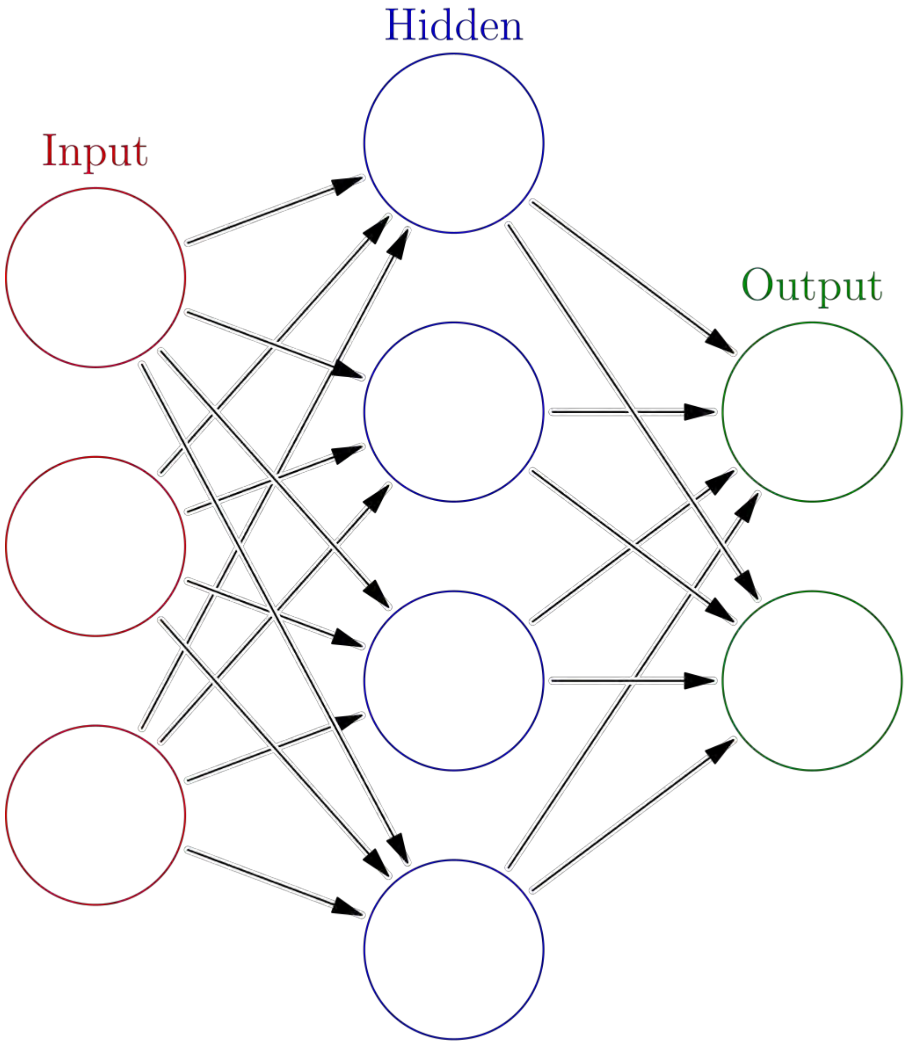
PMID: 34881096 PMCID: PMC8609286 DOI: 10.4103/jpi.jpi_23_21

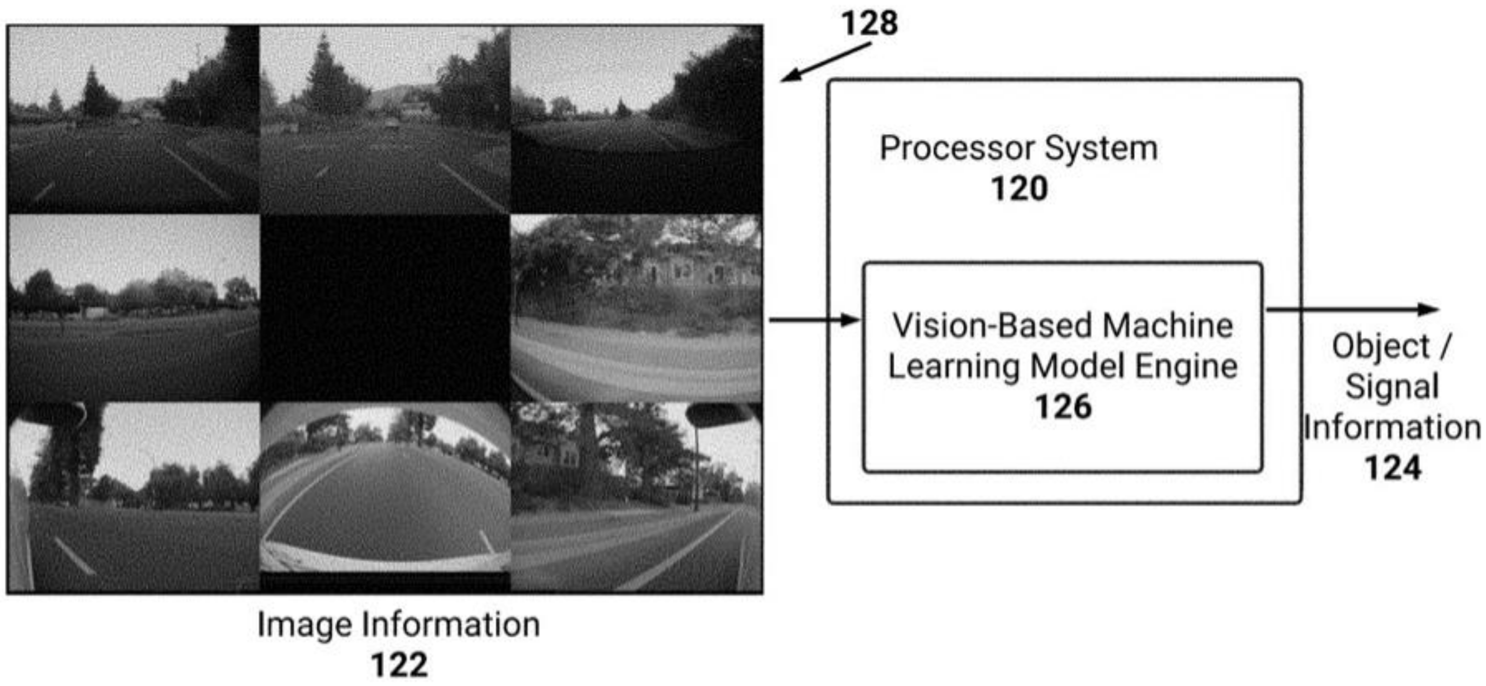
- Though this still relies on a limited pool of expert pathologists, for an increasing demand for assessment

AI, Neural Nets, Machine Learning, Etc

- Developments in computer learning, especially in the realm of pattern recognition, have seen significant advancement in the past 10 years
- Broadly, these will have application in various tasks and fields:
  - Image development
  - Language derivation and creation
  - Transportation
  - Medicine

General Topology of Neural Nets (AI) and Application





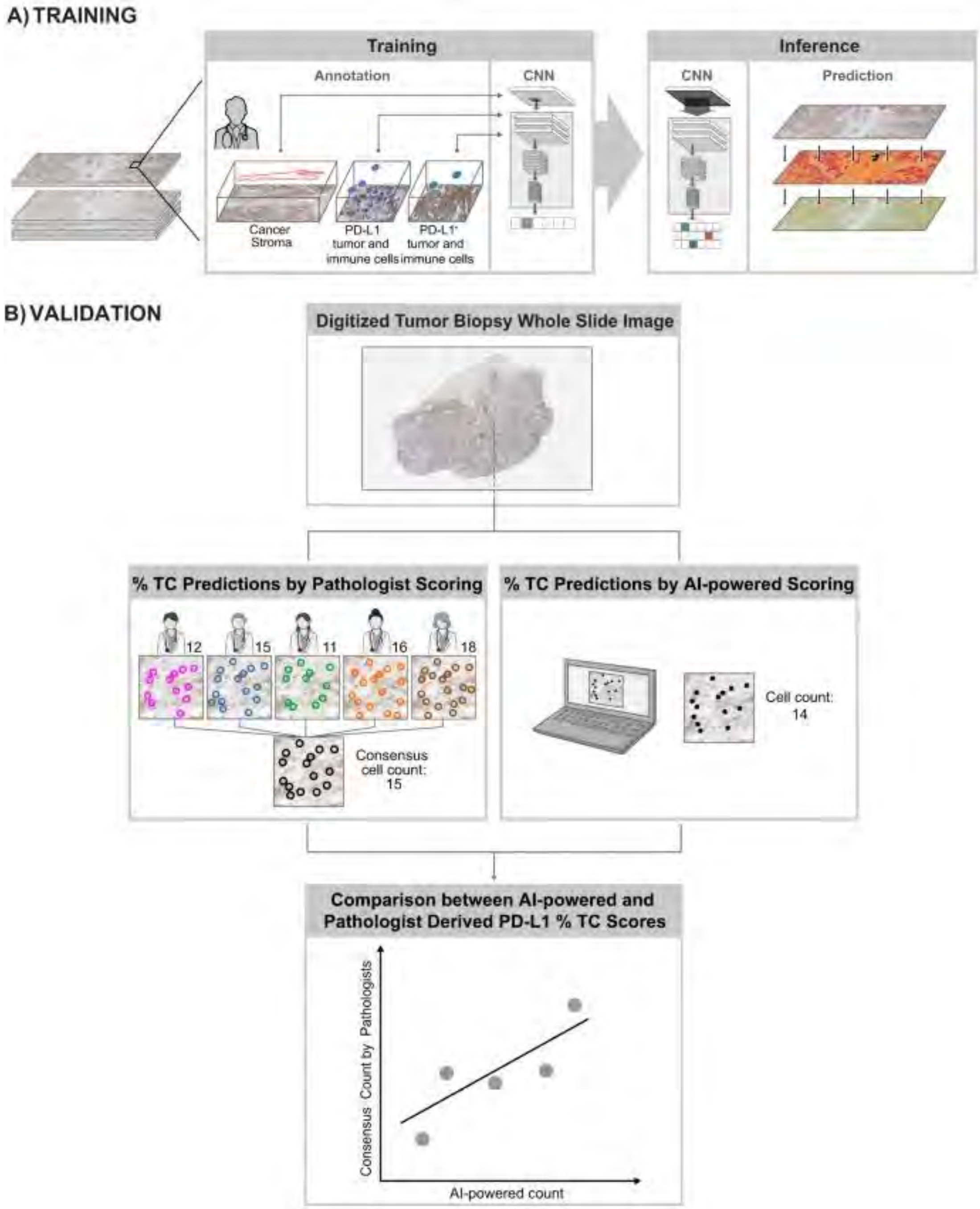
Application of AI in “real-world”

Article | Open access | Published: 15 July 2022

Association of artificial intelligence-powered and manual quantification of programmed death-ligand 1 (PD-L1) expression with outcomes in patients treated with nivolumab ± ipilimumab

Vipul Baxi, George Lee, Chunzhe Duan, Dimple Pandya, Daniel N. Cohen, Robin Edwards, Han Chang, Jun Li, Hunter Elliott, Harsha Pokkalla, Benjamin Glass, Nishant Agrawal, Abhik Lahiri, Dayong Wang, Aditya Khosla, Ilan Wapinski, Andrew Beck & Michael Montalto

Modern Pathology 35, 1529–1539 (2022) | Cite this article



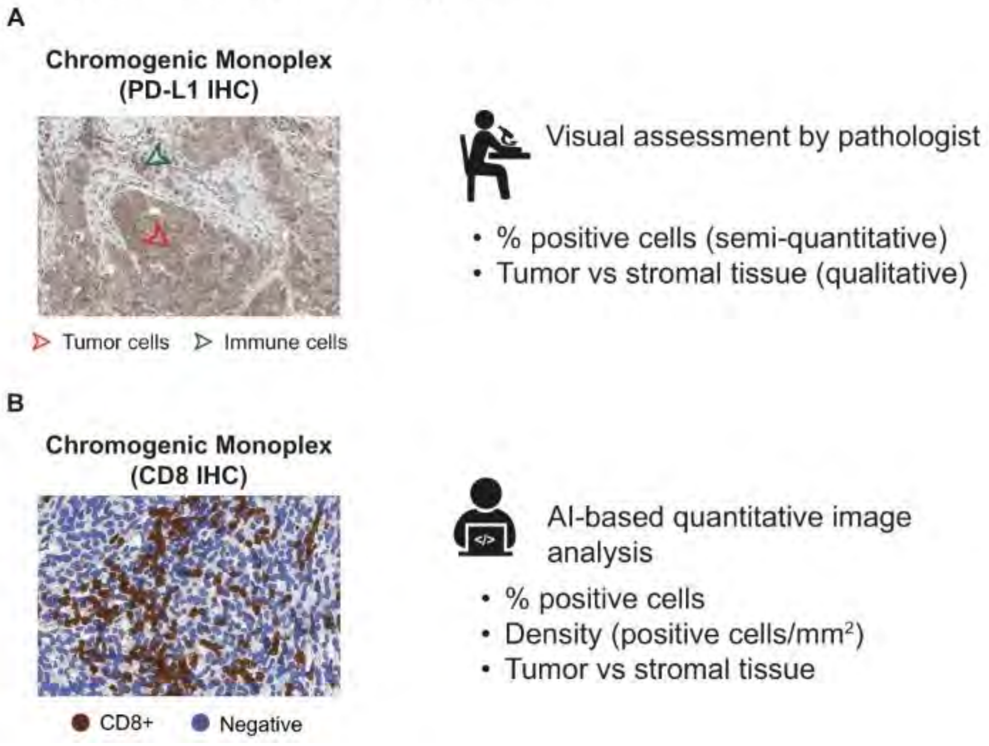
Review Article | Open access | Published: 05 October 2021

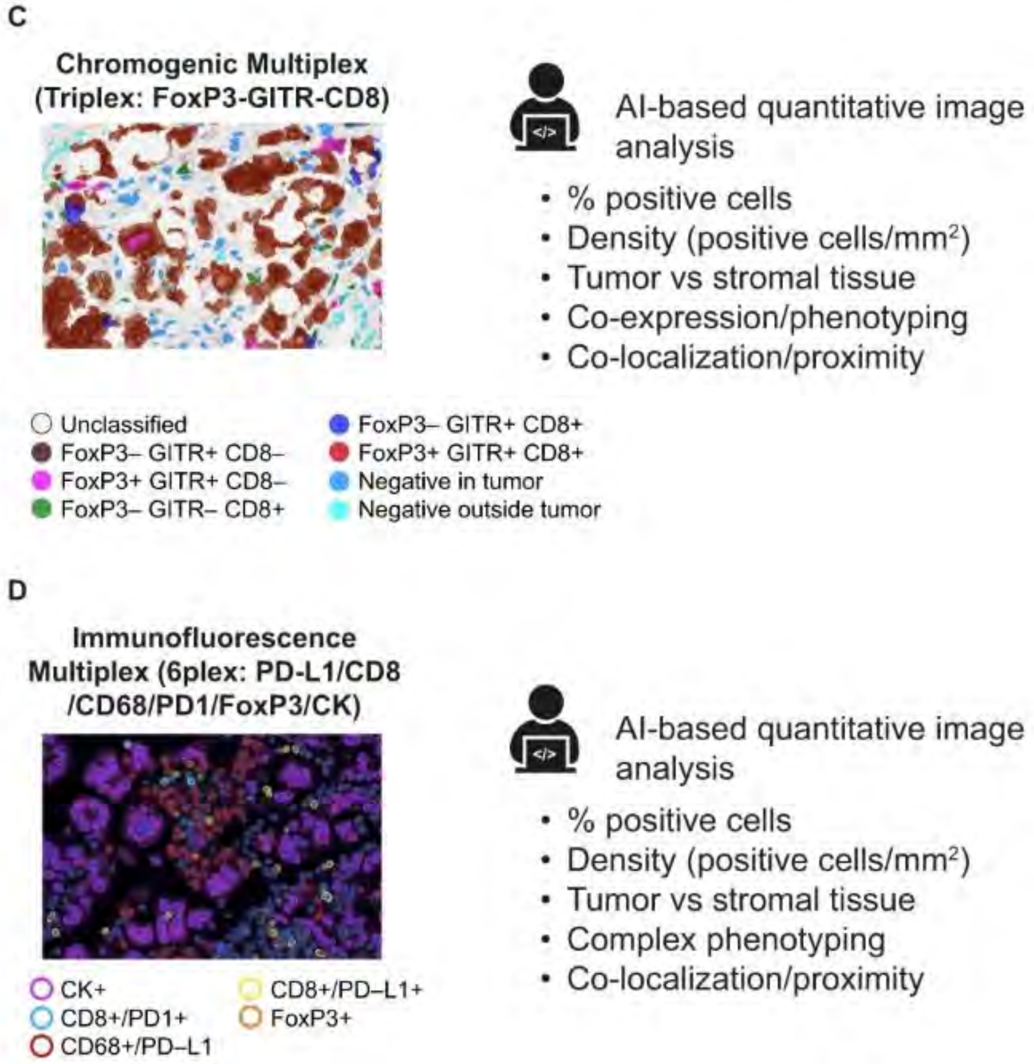
Digital pathology and artificial intelligence in translational medicine and clinical practice

Vipul Baxi, Robin Edwards, Michael Montalto & Saurabh Saha

Modern Pathology **35**, 23–32 (2022) | Cite this article

Fig. 3: Applications of digital pathology in IHC.





What about the Transplant Space?

bioengineering

MDPI

Systematic Review

Artificial Intelligence Advances in Transplant Pathology

Md Arafatur Rahman [1,2], Ibrahim Yilmaz [1,3], Sam T. Albadri [1], Fadi E. Salem [1], Bryan J. Dangott [1,3], C. Burcin Taner [4], Aziza Nassar [1] and Zeynettin Akkus [1,3,*]

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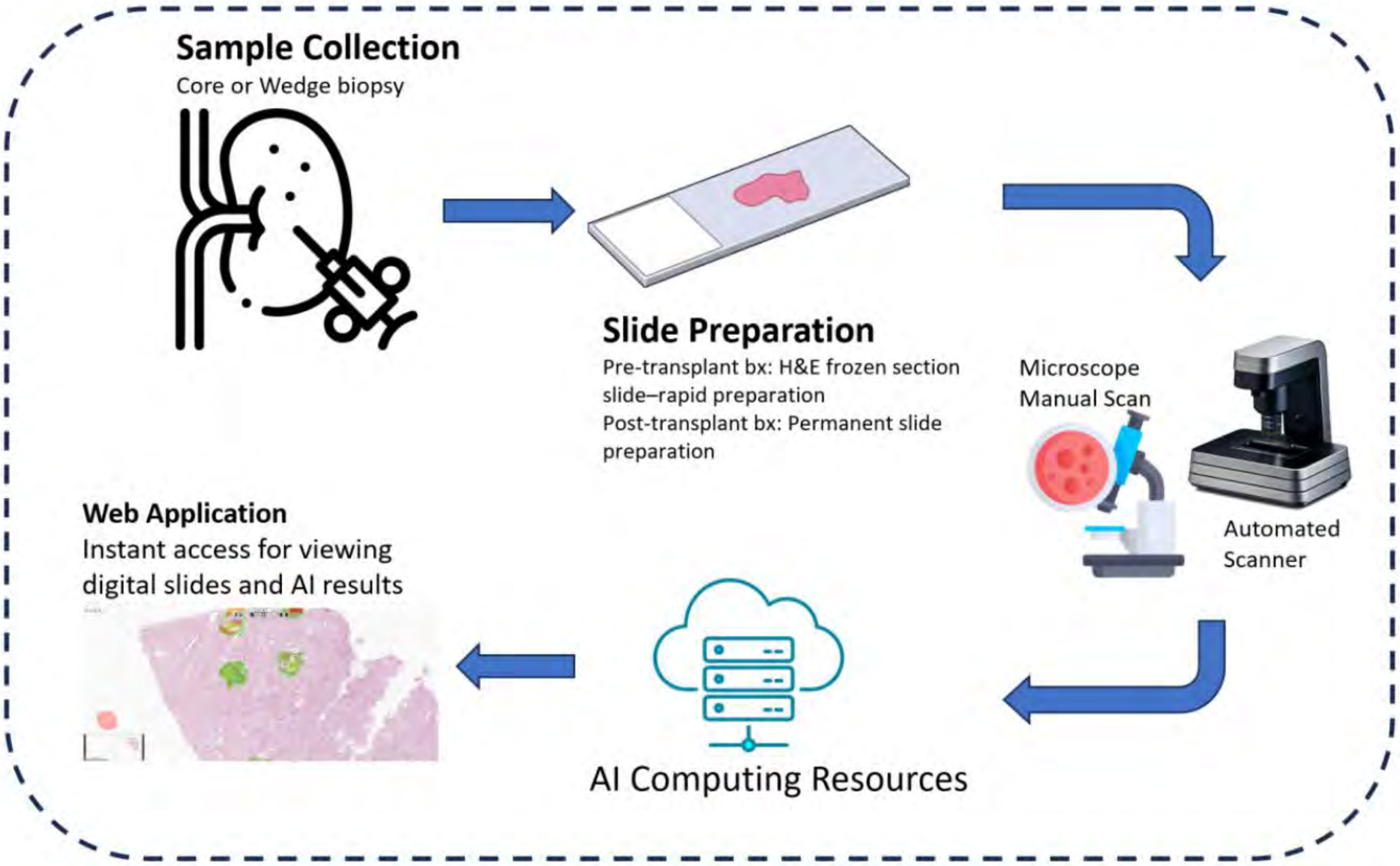
AI and Transplant

- Numerous studies have been published looking at the role of AI models to interpret whole slide imaging in transplant:

2. Peyster, E.G.; Arabyarmohammadi, S.; Janowczyk, A.; Azarianpour-Esfahani, S.; Sekulic, M.; Cassol, C.; Blower, L.; Parwani, A.; Lal, P.; Feldman, M.D.; et al. An Automated Computational Image Analysis Pipeline for Histological Grading of Cardiac Allograft Rejection. *Eur. Heart J.* **2021**, *42*, 2356–2369. [CrossRef]
3. Davis, H.; Glass, C.; Davis, R.C.; Glass, M.; Pavlisko, E.N. Detecting Acute Cellular Rejection in Lung Transplant Biopsies by Artificial Intelligence: A Novel Deep Learning Approach. *J. Heart Lung Transplant.* **2020**, *39*, S501–S502. [CrossRef]
4. Smith, B.; Grande, J.; Ryan, M.; Smith, M.; Denic, A.; Hermsen, M.; Park, W.; Kremers, W.; Stegall, M. Automated Scoring of Total Inflammation in Renal Allograft Biopsies. *Clin. Transplant.* **2023**, *37*, e14837. [CrossRef]
5. Liu, Z.; Liu, Y.; Zhang, W.; Hong, Y.; Meng, J.; Wang, J.; Zheng, S.; Xu, X. Deep Learning for Prediction of Hepatocellular Carcinoma Recurrence after Resection or Liver Transplantation: A Discovery and Validation Study. *Hepatol. Int.* **2022**, *16*, 577–589. [CrossRef]

AI and Transplant Potential

- Reduce inter-reader variability
- Better enable teleconsultation pre- /post-transplant biopsies
- Assessment of additional morphological parameters and special relationships
  - More reliably?
  - Resistant to fatigue?
  - Resistant to prior biases?


Sample Collection
Core or Wedge biopsy
Slide Preparation
Pre-transplant bx: H&E frozen section slide–rapid preparation
Post-transplant bx: Permanent slide preparation
Microscope Manual Scan
Automated Scanner
AI Computing Resources
Web Application
Instant access for viewing digital slides and AI results

Heart Transplant

Table 1. A summary of previous AI studies investigating transplant heart pathology.

Author, Year	Objective	AI Model	Dataset	Performance
Giuste et al., 2023 [14]	Enhancing risk assessment of rare pediatric heart transplant rejection through the generation of synthetic images	Progressive and inspirational GAN [17,18]	12 non rejection and 12 rejection slides	95.56% AUROC for biopsy level rejection detection with 83.33% sensitivity and 66.67% specificity
Lipkova et al., 2022 [15]	Assessment of cardiac allograft rejection from endomyocardial biopsies	Pre-trained deep residual CNN [19]	Training: 1352 WSI slides; Validation: 1840 WSI slides	Allograft reject detection with an AUC of 0.962
Peyster et al., 2021 [2]	Histological grading of cardiac allograft rejection	Computer-Assisted Cardiac Histologic Evaluation (CACHE) grader pipeline	2472 endomyocardial biopsy slides	Differentiate low- and high-grade rejection with an AUC of 0.83
Glass et al., 2020 [16]	Determine myocyte damage in cardiac transplant acute cellular rejection	Pre-trained VGG16 [20]	19,617 annotations (10,855 regions of ACR; 5002 healing injury; 3760 normal)	Detection of myocyte damage (Grade 1R2) from non-myocyte damage (Grade 1R1A) with 94% validation accuracy

- Studies via multiple AI approaches (Generative Adversarial Networks vs. Computational Neural Nets) show strong correlation with human derived diagnoses – with disadvantage of having access to fewer images

Kidney Transplant

Table 3. Summary of previous AI studies on transplant kidney pathology.

Author, Year	Objective	AI Model	Dataset	Performance
Hermsen et al., 2019 [32]	Multiclass segmentation of digitized kidney biopsy tissue sections	UNet [38]	Training: 40 WSIs; Validation: 20 WSIs (Home: 10; External Institution: 10)	Detected 92.7% of all glomeruli in nephrectomy samples with 10.4% false positives
Hermsen et al., 2022 [33]	Quantifying the chronic and inflammatory lesions in kidney transplant biopsies	UNet [38]	125 WSI pairs of periodic acid-schiff- and CD3-stained slides	The tissue class glomeruli was segmented with precision, recall, and dice scores of 0.96, 0.94, 0.95, respectively
Kers et al., 2022 [34]	Classifying histology of kidney allograft biopsies	Single CNN (InceptionV3) [46], Serial CNN	5844 WSIs from 1948 patients	AUROC (Single CNN) of 0.86, 0.78, and 0.70 for the normal and rejection disease classes, respectively
Smith et al., 2023 [4]	Quantifying the amount of non-glomerular inflammation within the cortex	UNet [38]	60 biopsies from 53 patients	Precision, recall, and dice scores for glomeruli identification were 0.888, 0.830, and 0.858, respectively
Wilbur et al., 2021 [39]	Identifying glomeruli on renal biopsy containing four stains from multiple institutions	Modified version of AlexNet	71 biopsies (Training: 52; Testing: 19)	Sensitivity of 90–93% for intra-institutional and 77% for inter-institutional dataset

Liver Transplantation

- Early studies have focused on the donor side of the tissue equation
  - One-third of donor livers are rejected due to histopathologic findings associated with early allograft dysfunction
- A computer vision AI platform was developed and compared to pathologist scores, and offered a more reliable predictor than established scoring systems

Narayan et al., 2022 [50]	Prediction of donor liver allograft steatosis and early post-transplantation graft failure	CVAI model consisting of Fully Convolutional Networks (FCN) [53] and UNet	25,494 images from 90 liver biopsies	CVAI peak mean IU 0.80; steatosis score median (CVAI 3% vs. pathologist 20%)

Donor Liver Frozen Section Assessment

- An algorithm was trained to predict steatosis in donor liver biopsy frozen sections (in percentage)
- Correlation coefficient and intraclass correlation coefficient for the AI model (0.85 and 0.85) surpassed the performance by on-service pathologists (0.74 and 0.72, respectively)

Sun et al., 2020 [52]	Quantify percent steatosis in donor liver biopsy frozen sections	Pre-trained VGG16 (truncated at bottleneck layer)	96 WSIs (Training: 30; Testing: 66)	r = 0.85, ICC = 0.85 on testing samples

Challenges and Future Implementations

- These technologies rely upon digitization of WSI and ingestion of these data into an AI model
  - Cost and access barriers will need to be overcome, especially in medical facilities with lower volume, less capital, etc
- Comparison amongst and between models is needed to continually improve outcomes
  - Could a model be developed wherein slides are routinely scanned and assessed, with comparison back to the original pathologist diagnosis to better improve the models
- How does one address the liability, legality and privacy of these types of models in the future
- How can we identify additional data to train our models?

(19) **United States**
(12) **Patent Application Publication**
Abfall et al.

(10) **Pub. No.: US 2024/0378899 A1**
(43) **Pub. Date: Nov. 14, 2024**

(54) **VISION-BASED SYSTEM TRAINING WITH SIMULATED CONTENT**

(71) Applicant: **Tesla, Inc.**, Austin, TX (US)

(72) Inventors: **David Abfall**, Austin, TX (US); **Michael Hosticka**, Austin, TX (US)

(73) Assignee: **Tesla, Inc.**, Austin, TX (US)

(21) Appl. No.: **18/684,607**

(22) PCT Filed: **Aug. 18, 2022**

(86) PCT No.: **PCT/US2022/040793**

§ 371 (c)(1),
(2) Date: **Feb. 16, 2024**

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filed on Dec. 9, 2021.

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G06T 7/13 (2006.01)
G06V 20/70 (2006.01)

(52) **U.S. Cl.**
CPC ***G06V 20/588*** (2022.01); ***G06T 7/13*** (2017.01); ***G06V 20/70*** (2022.01)

(57) **ABSTRACT**

Aspects of the present application correspond to utilization of a combined set of inputs from simulation systems to

Original Research

Explainable synthetic image generation to improve risk assessment of rare pediatric heart transplant rejection

Felipe O. Giuste [a], Ryan Sequeira [a], Vikranth Keerthipati [a], Peter Lais [a], Ali Mirzazadeh [b], Arshawn Mohseni [a], Yuanda Zhu [b], Wenqi Shi [b], Benoit Marteau [b], Yishan Zhong [b], Li Tong [a], Bibhuti Das [c], Bahig Shehata [d], Shriprasad Deshpande [e], May D. Wang [a b]

Clear and Ready Use for this Technology

- Clearly, a more objective and available approach, especially in pre-transplant assessment, would be in line with OPTN goals to increase organ utilization rates while maintaining / improving outcomes
- Access to digital imaging and scanners appropriate for frozen section assessment will be vital to applying these approaches going forward
- Will have ready impact in post-transplant settings to provide optimal diagnoses and assessments for more appropriate care for our patients