

Agreement between X-ray phase contrast imaging and conventional histopathology in the assessment of acute graft cellular rejection grading following heart transplantation

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RECEIVED:
October 13, 2024

ACCEPTED:
October 31, 2024



KEYWORDS: cellular graft rejection, endomyocardial biopsy, X-ray phase contrast imaging, histopathology.

CITATION: *Cardiol Croat.* 2024;19(11-12):516-7. | <https://doi.org/10.15836/ccar2024.516>

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Introduction: Acute cellular rejection (ACR) of the cardiac allograft is the clinically most relevant complication after heart transplantation (HTx). Light microscopy-based histopathology diagnosis (PHD) of endomyocardial biopsy tissue (EMB) is the golden standard in post-HTx follow-up. Recent studies have demonstrated the application of X-ray phase-contrast imaging (X-PCI) in cardiac tissue imaging, enabling 2D and 3D virtual histopathology^{1,2}.

Methods: 152 EMB samples were collected prospectively at multiple timepoints from 75 Htx recipients in two clinical centres (University Hospital centre Zagreb and Dubrava University Hospital), imaged by X-PCI at the Paul Scherrer Institute TOMCAT beamline (Villigen, Switzerland) with an established imaging protocol³ (average of 6678 images per sample at 0.65 µm pixel size), and then prepared for PHD analysis with light microscopy. Three image datasets of digitalized standard PHD 2D slides, X-PCI 2D images, and X-PCI 3D whole sample scans were prepared for the ACR grade analysis by a pathologist in a blinded fashion based on the ISHLT 2004. criteria. Agreement between methods was assessed using Cohen's weighted kappa, with clinically relevant grades (2R and 3R) carrying increased magnitude of weight in the calculations.

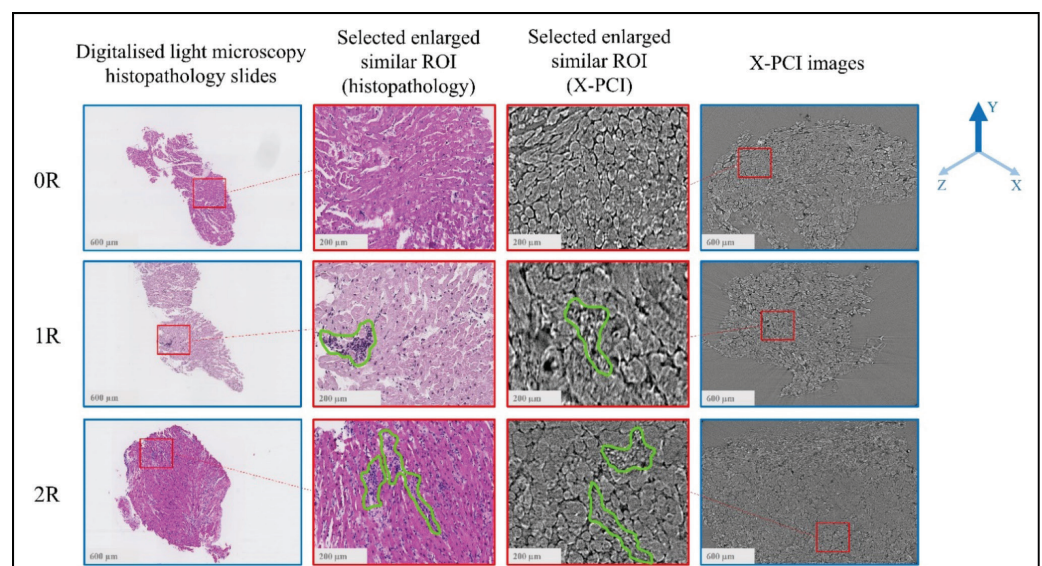


FIGURE 1. Comparison between digitalised histopathology slides and X-PCI images with selected similar regions of interest of the same sample (0R, 1R and 2R rejection grade). ROI = region of interest; X-PCI = X-ray phase contrast imaging.

Results: A comparison of digitalized PHD slides and X-PCI images of samples with different ACR grades is shown in **Figure 1**. Majority of samples (83.56%) did not show a clinically relevant grade of rejection in all 3 datasets (0R in 76.32% and 1R in 7.24% of samples), 15.79% of samples had 0R and 1R grade variation between datasets, and one sample had a significant 2R grade. Conventional PHD grading showed substantial agreement with both 2D X-PCI ($\kappa = 0.63$, 95% CI: 0.41-0.84) and 3D X-PCI histopathology ($\kappa = 0.61$, 95% CI: 0.40-0.82), with the highest level of agreement ($\kappa = 0.78$, 95% CI: 0.64-0.92) achieved comparing 2D and 3D X-PCI analyses.

Conclusion: A high level of agreement was achieved when comparing 2D and 3D X-PCI virtual histopathology with conventional PHD analysis in ACR grading. X-PCI is a non-destructive method that enables whole EMB sample scanning to assess ACR grading, showing potential for future application in HTx follow-up.

Supported by the Croatian Science Foundation (research grant GRAFT-XPCI HRZZ-IP-2020-02-5572).

LITERATURE 

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