Thesis Project Portfolio

Accurate and Accessible Organoid Analysis with OrganoSeg2

(Technical Report)

Respect for Persons and the Dilemma of Control in Informed Consent for Organoid Research

(STS Research Paper)

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Sociotechnical Synthesis

Organoids are three-dimensional biological models that replicate the structure and function of organs, at a miniature scale (Tang et al., 2022). Organoids are valuable for studying human disease and treatments; however, they present technical and social challenges. Technically, organoids' three-dimensional environment complicates image analysis, necessitating organoid specific analysis platforms. Several machine-learning programs have developed for this task, but they are difficult to use for many researchers due to requisite training data or coding experience. My technical research involved the development of an application for organoid image analysis, improving accuracy and utility while maintaining an emphasis on usability. Socially, organoids are highly complex and present uncertainties in regards to their future uses and intrinsic moral value. My STS research investigated the current regulation for informed consent in the use of human-derived organoids and other biospecimens, and identified strategies for changing these policies to better respect human subjects. The overarching problem in my STS and technical research is that oversights on certain human aspects of research limit the accessibility and potential for scientific research.

The technical project expanded on an existing application called OrganoSeg (Borten et al., 2018), which segments images to collect data on organoid size and shape. This data collection is crucial in quantifying organoid performance when modeling disease or testing treatment. OrganoSeg is a popular tool requiring little prior knowledge, but it has limitations in accuracy, efficiency, and functionality. In this project, I created OrganoSeg2 to address the limitations of the original while maintaining the user-friendly platform, and sought to validate its effectiveness. After making changes to the segmentation algorithm, I compared the accuracy of OrganoSeg

with relevant alternatives. OrganoSeg performed comparably to other segmenting platforms across five organoid types, showing generalizability. Additionally, I implemented new features for downstream analysis that provide a more complete representation of organoid development. We applied these tools to monitor cell death in patient-derived breast cancer organoids in response to radiation treatment. We successfully developed a pipeline for analyzing organoids in this manner, and identified heterogeneities in response to treatment across patients. This experiment demonstrated the potential for biological findings that were not previously possible with a user-friendly interface.

The problem surrounding my STS research is that current regulations for biospecimens are insufficient in respecting the rights of human subjects, which excludes people from participation in research and is damaging to the relationship between researchers and the public. Further, the newness and complexity of organoid research presents more potential to infringe on donor values, yet regulation is not updating alongside the changing research landscape. I determined stakeholder values by examining responses to proposed regulatory changes and interviews about informed consent for biospecimens and organoids. Researchers and patients stress the need for unhindered research (*COGR, 2016)*. Alternatively, the public desires transparency and autonomy when donating specimens, often stemming from diverse experiences with medical institutions. However, these concerns are frequently overlooked (Kraft et al., 2019). I attempted to address these concerns through strategies such as reframing public values so they are met with greater consideration. I also suggested making incremental changes as opposed to sweeping overhauls. This would mitigate the risk to life-saving research while demonstrating greater respect for patients.

My technical research successfully improved an organoid segmentation platform and demonstrated its usability in a research project. The platform requires a larger number of parameters than the original, so it is important to document these well and consult users so that they do not impede usability. Additionally, the new features should be applied to different research pipelines to validate their usability in settings external to our lab, which may have different experimental practices. For my STS research, I was able to discuss values that are important for organoid donors and present strategies for creating and implementing new informed consent procedures, but I did not reach a solution on the ideal model for informed consent. As organoid research grows, there will be more public perspectives representing diverse groups, and these donor values should be identified using the strategies I discussed. Additionally, more thorough consent procedures should be implemented and monitored for their effect on public opinion and research, ensuring that this process is a compromise.

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