INTRODUCTION
Revolutionizing Neuroimaging Research with Highly Portable MRI: Confronting Ethical and Legal Challenges

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Keywords: Portable MRI, Neuroscience Research, Neuroimaging, Research Ethics

Roughly a decade ago, then-President Obama launched the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative to make progress on one of the most challenging scientific problems — understanding how the human brain and nervous system work.[1] Based at the National Institutes of Health (NIH), the BRAIN Initiative has funded and catalyzed breakthrough technologies and studies to make progress in addressing this enormous challenge. Yet neuroscience research has long been hampered by the historical failure to reach all populations and ensure their inclusion in research. The result has been non-representative datasets and a failure to partner with individuals and communities essential to progress.

Community-engaged magnetic resonance imaging (MRI) research projects remain limited in number and scope.[2] For over a decade "[r]esearchers in both social and biological sciences have pointed to the negative consequences of extrapolating from small, nonrepresentative samples based on the systematic biases these samples can introduce."[3] This "[b]iased sampling in neuroimaging research can fundamentally distort our understanding of brain–behavior relationships."[4]

As the BRAIN Initiative has progressed, a new set of technologies has emerged with the potential to revolutionize brain research and transform our understanding of brain function in health and disease. In 2020, the U.S. Food and Drug Administration (FDA) approved a new type of magnetic resonance imaging (MRI) scanner that was far smaller, less expensive, and more portable than the large, traditional MRI machines typically bolted to the facility's floor in a dedicated scanning suite.[5] The scanner approved by the FDA was one of a suite of new, highly portable MRI (pMRI) machines that have since emerged with a range of imaging power and specifications.[6]

What unites these pMRI scanners is the capacity to scan anywhere — in remote villages, in school gymnasiums, in a van, in a skilled nursing facility, and even right outside the participant's home. This distinguishes these new machines from fixed MRI scanners, which by design are locked behind secure doors and hard for the community to access. These new pMRI capabilities mean that brain research can now reach communities previously underrepresented in neuroscience studies. Against this backdrop, pMRI holds the potential to generate a paradigm shift in neuroimaging research.[7] Instead of research participants traveling to the scanner, now the scanner can come to them.

However, many of these same communities may also have poor access to health care, may face barriers to neurological care for problematic research results and incidental findings, and may have war-

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The Journal of Law, Medicine & Ethics, 52 (2024): 764-768. DOI: 10.1017/jme.2024.161

ranted concerns over exploitative research. Moreover, pMRI scanners are smaller and more portable than traditional MRI machines in part because some of the scanner's functionality is managed remotely. The pMRI scanner may acquire data that is then transmitted to a cloud platform, where the lower resolution of some pMRI machines requires complex processes to produce an image, often aided by artificial intelligence. Ultimately, the data may be transmitted to and analyzed by researchers far from the site where participants are scanned. The pMRI scanner is thus only the most visible part of a set of technologies that are combined to enable distant researchers to analyze the research participants' brain structure and function.

Greater portability and accessibility will allow pMRI researchers to work with communities to develop novel neuroimaging research designs, while permitting researchers who have not previously utilized MRI in their studies to do so. By reaching communities that have been traditionally underrepresented in MRI research, pMRI research may contribute to understanding the representative brain through population neuroscience, improve screening for brain health, and facilitate neuroimaging participation with greater racial, ethnic, geographic, and socioeconomic diversity.[8] In short, pMRI may transform the future of neuroimaging research by radically altering where scans are occurring and who is doing the scanning.

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However, this promising future requires careful attention to challenging ethical, legal, and societal implications (ELSI). Along with the potential to reach new populations — building an accurate understanding of the true range of brain structure and function in human beings who are healthy and those who are not — pMRI brain scanning in remote field settings poses serious risks and challenges. To analyze those challenges and recommend solutions, we convened a multidisciplinary Working Group (WG) funded by a grant from the NIH BRAIN Initiative (*Highly Portable and Cloud-Enabled Neuroimaging Research: Confronting Ethics Challenges in Field Research with New Populations,* NIH RF1MH123698).

Hosted by the University of Minnesota's Consortium on Law and Values in Health, Environment & the Life Sciences, the WG included experts from fields including neuroscience, engineering, physics, ethics, and law. The project also featured a national conference in 2023 on "Emerging Portable Technology for Neuroimaging Research in New Field Settings: Legal & Ethical Challenges." The conference included discussion of community engagement, data control, and oversight in pMRI research. The WG published its detailed analysis of 15 core pMRI research ELSI issues along with recommended solutions.[9] We then took the next step — formulating operational recommendations, an empirical analysis, plus more targeted individual articles on specific issues written by project members and their coauthors.

This Symposium is the result. Our project group offers eight articles covering a wide swath of issues raised by the revolutionary potential and the ELSI challenges of pMRI research. The first article, "Conducting Research with Highly Portable MRI in Community Settings: A Practical Guide to Navigating Ethical Issues and ELSI Checklist," is a WG consensus product that goes beyond our previously published recommendations by offering a roadmap for implementation.[10] Traditional MRI facilities are familiar with checklists to ensure safe scanning. We go a step further to offer a *Portable MRI Research ELSI Checklist*. The Checklist was developed through extensive WG discussion and consideration of the real-world needs of MRI researchers. It provides pMRI investigators, both those already using the technology and those considering adopting it, with concrete guidance for conducting pMRI research in the community. The Checklist provides guidance over the lifecycle of a research project and emphasizes the centrality of community engagement throughout the research process. Community-engaged MRI research can be one of pMRI's most valuable contributions. But to realize that potential will require neuroscience researchers to revisit current practice and learn from community-engagement strategies successfully deployed in related fields. This first article provides much-needed guidance and resources for neuroscientists to advance toward community-engaged pMRI research.

The second article in this Symposium, authored by psychologist Molly Madzelan and Professors (and Project PIs) Frances Lawrenz, Susan Wolf, and Fran-

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cis Shen on "Expert Stakeholder Perspectives on Emerging Technology for Neuroimaging Research with Highly Portable MRI: The Need for Guidance on Ethical, Legal, and Societal Issues," presents results from the first survey of expert stakeholders on ELSI issues posed by pMRI and other portable neuroimaging technologies.[11] Survey respondents included "(1) researchers using MRI or developing new hardware and software; (2) neuroethics and legal scholars; (3) neuroimaging and radiology industry professionals; (4) leaders in standard-setting professional organizations; (5) representatives from patient advocacy organizations; (6) insurance professionals; (7) experts in relevant legal issues such as HIPAA; and (8) relevant experts in regulation and relevant regulators themselves."[12] The survey revealed stakeholder concern for participant safety and participants receiving alarming or inaccurate results. The survey also found that stakeholders prioritized solutions such as setting up quality assurance mechanisms and establishing clear policies for when to return incidental findings (IFs).

The articles in this Symposium — together with the additional work of our project — lay the foundation for conducting ethical and scientifically rigorous pMRI research in field settings with new and underrepresented populations.

A striking finding was that most experts are not yet very familiar with pMRI technologies and how they can be deployed in research. The article thus emphasizes the urgent need to inform stakeholders about pMRI—both its promises for research and its ethical and legal risks.

Professors Susan Wolf and Judy Illes then tackle the vexing challenge of IFs in pMRI research in "Far from Home: Managing Incidental Findings in Field Research with Portable MRI".[13] Wolf and Illes analyze the question of how to manage IFs that may warrant clinical work-up when the research is conducted in the field, far from a hospital, and in communities without ready access to clinical care. The authors argue that the duty to manage IFs remains and they urge working with the community to create an acceptable plan. The authors argue that researchers owe participants from historically underserved and under-resourced communities at least as much access to information about IFs as would be offered to participants without those challenges. The article presents guidance on co-creating an IFs plan that provides a timely pathway to care, avoids exploitation, and offers local value to participants.

As pMRI moves beyond the lab and into the real world, it could facilitate research with Indigenous communities. The interdisciplinary team of bioethicist Shana Birly, engineer Angela Teeple, and Professor Illes explore the ethical challenges associated with such research in "The Realization of Portable MRI for Indigenous Communities in the USA and Canada."[14] This pathbreaking article focuses on Native American People in the United States and Indigenous People in Canada (First Nation, Métis, Inuit), and provides guidance on how to improve neuroscience researchers' cultural sensitivities so that pMRI research with Indigenous populations will better meet the needs and preferences of historically neglected Indigenous communities. Solutions include engaging local leadership and communities, and empowering pMRI researchers to better appreciate and incorporate the perspectives of Indigenous communities.

In "Socioeconomic Factors in Brain Research: Increasing Sample Representativeness with Portable MRI," Professor Martha Farah explores the potential for pMRI research to redress historical underrepresentation of participants with lower socioeconomics status (SES) in neuroimaging research.[15] Farah discusses the value that pMRI research with lower SES communities could provide, and the barriers to carrying out such studies. Farah cautions against the danger of biological essentialism and stresses the importance of ethical guidance on when and how to conduct and report comparative analyses of brain structure based on SES. Her article suggests how researchers considering pMRI research with populations challenged by lower SES can minimize the likelihood that their findings will be misused.

Professors Eran Klein, Duke Han, Paul Tuite, Taylor Kimberly, and Mohit Agarwal next explore the emerging application of pMRI in dementia research.[16] As the global population ages, the incidence of dementia is increasing, with treatments sorely needed. One promising research strategy is to study early brain changes from before symptom onset, and pMRI could help accomplish this, ushering in a new wave of dementia neuroimaging studies. In "Portable Accessible MRI in Dementia Research: Ethical Considerations About Research Representation and Dementia-Friendly Technology" the authors describe how pMRI could catalyze new dementia research, and they examine

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the implications, including for oversight, safety, and diversity of research participants. The authors emphasize the need for pMRI technologies to be dementia-friendly and person-oriented.

Oversight will be critical in addressing the ethical issues associated with pMRI research. In "The Need for IRB Leadership to Address the New Ethical Challenges of Research with Highly Portable Neuroimaging Technologies," Drs. Donnella Comeau, Benjamin Silverman, and Mahsa Alborzi Avanaki with Professor Wolf argue that the coming democratization of neuroimaging through pMRI research calls for IRBs to expand their traditional scope.[17] The article urges that well-resourced IRBs with a history of overseeing MRI research play a leadership role not only for pMRI research by affiliated investigators but also for research by unaffiliated external researchers in the community. Some of those external researchers will be individuals and groups who are able to conduct brain research for the first time thanks to the greater accessibility and portability of pMRI scanners. And a subset of that research may not be covered by the federal Common Rule for research with human participants.[18] However, the authors argue that oversight is essential and that experienced IRBs have a crucial role to play. Indeed, the authors argue that IRBs should go beyond their traditional limits to consider potential social harms from pMRI research. This innovative vision for IRBs can help ensure the development of effective guardrails for the wide range of pMRI research that will likely emerge.

In the final article, "Ethical Oversight and Social Licensing of Portable MRI Research," Professor Barbara Evans examines two questions: (1) how existing U.S. privacy and research ethical frameworks will apply to pMRI research, and (2) what regulatory gaps exist in ensuring that pMRI research is conducted ethically with socially beneficial ends.[19] This analysis of the legal and regulatory frameworks governing pMRI research is essential reading for pMRI researchers, IRB personnel, regulators, and counsel at institutions pursing pMRI research. Professor Evans finds that the regulatory frameworks that will apply to most pMRI research were not designed to ensure that pMRI research will benefit the public. She suggests new regulation that would require pMRI (and other) research be approved by the public through a "social license" for research.

The articles in this Symposium — together with the additional work of our project — lay the foundation for conducting ethical and scientifically rigorous pMRI research in field settings with new and underrepresented populations. The articles make clear that community and public engagement are essential to address the ELSI challenges posed by pMRI research. Portable MRI holds tremendous potential to revolutionize brain research and reach new populations and researchers. The key to accomplishing that goal lies in partnership with the individuals and communities whose participation in neuroscience research is sorely needed.

Acknowledgements

Preparation of this article was supported by National Institute of Mental Health, National Institutes of Health grant RF1MH123698 (Shen, Wolf, Lawrenz, PIs). The views expressed in this article are those of the authors and not necessarily those of the funders. We thank Dori Henderson, Ph.D., for expert management of this Symposium. We also thank Melissa Hartley and Ian Stevens for valuable research assistance on this introduction.

Disclosures

The authors have no relevant disclosures.

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