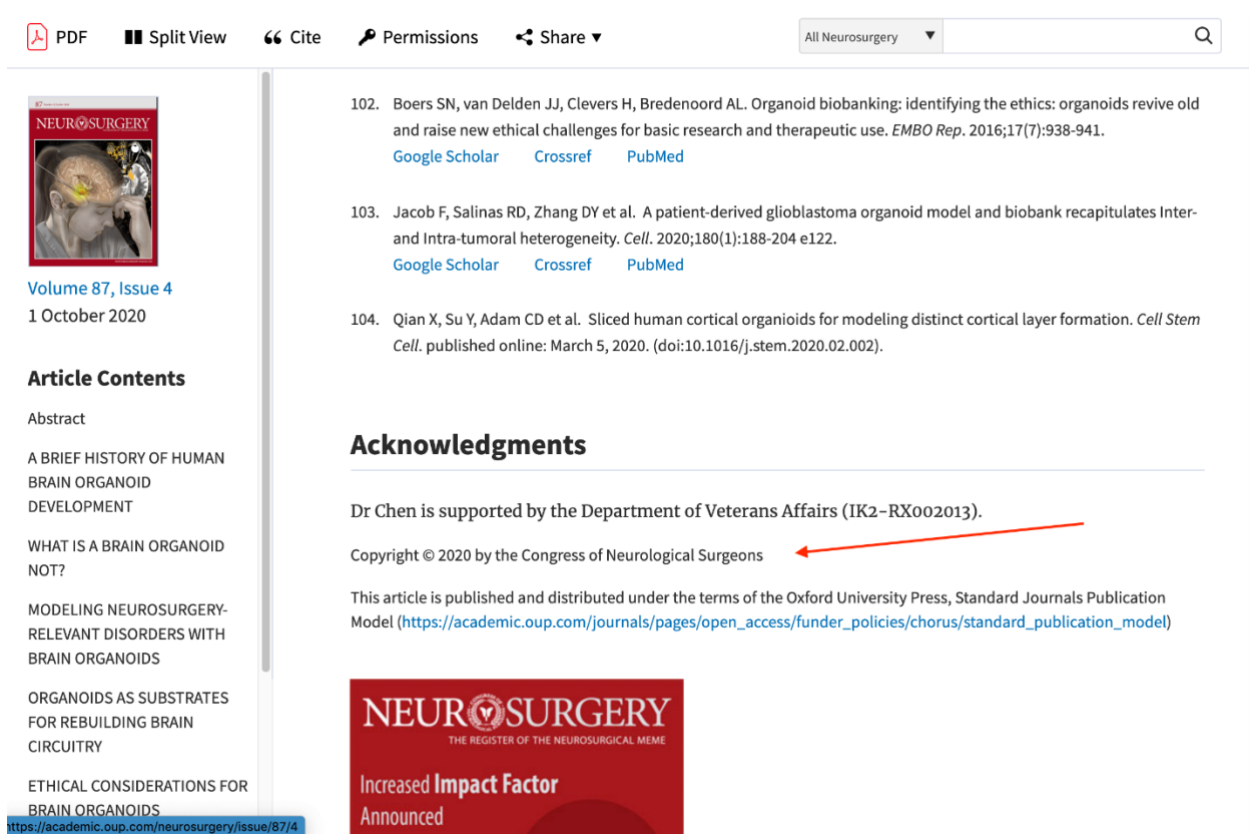


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## A Primer on Human Brain Organoids for the Neurosurgeon

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Human brain organoids emerged in 2013 as a technology that, unlike prior *In Vitro* neural models, recapitulates brain development with a high degree of spatial and temporal fidelity. As the platform matured with more accurate reproduction of cerebral architecture, brain organoids became increasingly valuable for studying both normal cortical neurogenesis and a variety of congenital human brain disorders. While the majority of research utilizing human brain organoids has been in the realm of basic science, clinical applications are forthcoming. These present and future translational efforts have the potential to make a considerable impact on the field of neurosurgery. For example, glioma organoids are already being used to study tumor biology and drug responses, and adaptation for the investigation of other neurosurgery-relevant diseases is underway. Moreover, organoids are being explored as a structured neural substrate for repairing brain circuitry. Thus, we believe it is important for our field to be aware and have an accurate understanding of this emerging technology. In this review, we describe the key characteristics of human brain organoids, review their relevant translational applications, and discuss the ethical implications of their use through a neurosurgical lens.

**KEY WORDS:** Brain organoids, Brain repair, Disease models, Glioblastoma, Stem cells

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**H**uman brain organoids are a growing technology that has garnered significant attention in the scientific community and public domain. These *In Vitro* constructs exploit the self-organizing properties of pluripotent stem cells (PSCs) to recapitulate key steps during neurodevelopment, resulting in neural tissues with a surprising degree of similarity to the human brain.<sup>1</sup> Two categories of brain organoids have been generated. Whole-brain organoids, dubbed “mini-brains” by the press, exhibit a variety of cerebral structures, ranging from cortical to choroid plexus to cerebellar tissues.<sup>2</sup> More recent work has established protocols for creating region-specific

and retina.<sup>3–10</sup> These achievements have raised the possibility that human brain tissue could be wholly generated and studied in the laboratory, free from the constraints of the operating room or autopsy suite. Such a platform could enable study of human neurodevelopment and disease in previously unimaginable ways.

Much of the research involving brain organoids remains in the realm of basic science, but clinical applications utilizing this technology are on the horizon.<sup>11</sup> These applications include modeling neurosurgery-relevant diseases and disorders, such as glioblastoma, and repairing brain circuitry after damage following traumatic brain injury, stroke, and surgical resection. As

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### Abstract

Human brain organoids emerged in 2013 as a technology that, unlike prior in Vitro neural models, recapitulates brain development with a high degree of spatial and temporal fidelity. As the platform matured with more accurate reproduction of cerebral architecture, brain organoids became increasingly valuable for studying both normal cortical neurogenesis and a variety of congenital human brain disorders. While the majority of research utilizing human brain organoids

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