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Navigating the clinical trial pathway for implantable brain-computer interfaces: the COMMAND study

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***Introduction**:* Implantable brain-computer interfaces (BCIs) can enable people with paralysis to control digital devices using decoded brain signals. Predominantly, implantable BCIs have required craniotomy to place penetrating or surface electrodes on the brain, with some of these systems depending on transcutaneous ports for connectivity, leaving components visible and outside of the body. The Synchron BCI is a fully implanted system delivered using a minimally invasive endovascular technique. Following a first-in-human study completed in Australia (SWITCH trial[1]; n=4 participants), we present the results of the COMMAND early feasibility study — the first FDA-approved trial of a permanently implanted BCI — along with key insights gained from the clinical trial pathway.

***Material, Methods, and Results**:* The COMMAND study (ClinicalTrials.gov registration: NCT05035823) was a prospective, multi-center, single-arm, open label, early feasibility study (EFS) conducted under an investigational device exemption (G210178). The COMMAND EFS evaluated the safety and feasibility of the Synchron BCI in six participants with chronic severe bilateral upper limb paralysis. The primary endpoint was device related serious adverse events resulting in death or permanent increased disability. Secondary endpoints were device migration and target vessel patency. Additional outcomes explored BCI decoding of neural signals to generate 'digital motor outputs' for digital device control.

All six participants were successfully implanted with the endovascular BCI. Each participant met the primary study endpoint with no device related adverse events resulting in death or permanent increased disability during the one-year post-implant evaluation period. Additionally, there was preserved target vessel patency and no evidence of device migration at 3- and 12-months post-implant. Four out of six participants demonstrated consistent BCI decoding performance, enabling them to successfully perform various digital device control tasks throughout the one-year post-implant evaluation period. Of the remaining two participants: one experienced rapid progression of ALS leading to the withdrawal of life-sustaining care and the other encountered system signal artifacts, both of which impacted their ability to effectively use the BCI.

Conclusion: Endovascular access to brain regions for the placement of BCI sensors is an alternative to procedures requiring open-brain surgery. In addition to the favorable safety profile of endovascular procedures, the prevalence of angiography suites and neurointerventionalists capable of performing these procedures could promote wider and more rapid translation of BCI for people with paralysis. Results from the COMMAND EFS demonstrate early indication of safety and effectiveness of Synchron's endovascular BCI for participants with severe bilateral upper limb paralysis. Results and learnings from this study will contribute to the clinical translation of implantable BCIs via the clinical trial pathway.

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1. Mitchell, P. *et al.* Assessment of Safety of a Fully Implanted Endovascular Brain-Computer Interface for Severe Paralysis in 4 Participants: The Stentrode With Thought-Controlled Digital Switch (SWITCH) Study. *JAMA Neurol* **80**, 270 (2023).

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