

Supplementary Material

Supplementary Table 1. A, Human patient demographics and B, Cortical vein diameters.

| A. Patient demographics | | | |
|--------------------------------|----------------------|--|--|
| Number | n=50 | | |
| Age [mean, range] | 34.5 [18 – 73] years | | |
| Sex | Female 30/50 (60%) | | |

| B. Cortical Vein Presence and Diameters | | | |
|--|-----------------------|-----------------------|-----------------------|
| Sulcal Vein | Pre-central | Central | Post-central |
| Presence (at least one hemisphere) | 33/50 (66%) | 39/50 (78%) | 36/50 (72%) |
| Total no. veins | 41 | 48 | 41 |
| No. (%) left | 24 (59%) | 21 (44%) | 23 (56%) |
| No. (%) right | 17 (41%) | 27 (56%) | 18 (44%) |
| Proximal diameter (median and range) | 4.8 mm (2.9 – 7.5 mm) | 4.9 mm (3.6 – 8.5 mm) | 4.8 mm (3.4 – 6.1 mm) |
| Mid diameter (median and range) | 3.3 mm (2.2 – 4.6 mm) | 3.1 mm (2.2 – 4.5 mm) | 3.5 mm (2.5 – 5.3 mm) |
| Distal diameter (median and range) | 2.3 mm (1.7 – 3.7 mm) | 2.3 mm (1.6 – 4.5 mm) | 2.7 mm (1.8 – 5 mm) |

Supplementary Table 2. A, Sheep demographics and B, Vein and sinus diameters. Blood vessel measurements from cerebral venograms (n=28) and concurrent MRI brain scans with contrast (n=13), to characterize cerebral vein diameters.

| A. Sheep demographics | |
|---|---------------------|
| Sheep | n=33 |
| Age [mean, range] | 4.3 [2.5 – 5] years |
| Sex | Female 33/40 (83%) |
| Species | Sheep, Corriedale |
| Weight [mean, range] | 52 [50 – 57] kg |
| Horn to horn distance [median, interquartile range] | 7.75 [7.1 – 8.4] cm |
| Frontal ridge to occipital protuberance [median, interquartile range] | 12 [11.5 – 12.5] cm |

| B. Vein and Sinus Diameters | |
|------------------------------------|--|
| Vessel | Vessel Diameter (mm) Median [IQR] |
| Common Jugular Vein | 7.4 [6.2 – 8.6] |
| Internal Jugular Vein | 4.4 [3.5 – 6.1] |
| Transverse Sinus | 2.5 [1.9 – 3.4] |
| Superior sagittal sinus - proximal | 2.4 [2.4 – 2.5] |
| Superior sagittal sinus - middle | 1.7 [1.6 – 1.8] |
| Superior sagittal sinus - distal | 1.2 [1.0 – 1.5] |

Supplementary Table 3. Catheter identifier. Entire range of catheters used to optimize delivery of stentrode. Devices used in force testing are denoted with (*).

| Catheter identifier | Catheter model | Company | Internal diameter mm (inch) | External diameter (max) French, mm (inch) |
|----------------------------|-----------------------|----------------|------------------------------------|--|
| 6F (sheath) | Neuron Max 088 | Penumbra | 2.40 (0.088") | 8F, 2.67 (0.107") |
| *6F | Neuron 070 | Penumbra | 1.78 (0.070") | 6F, 2.00 (0.080") |
| *5F | Chaperone Guide | Stryker NV | 1.50 (0.059") | 5F, 1.70 (0.068") |
| 5F-B | DAC 057 | Stryker NV | 1.40 (0.057") | 5.2F, 1.75 (0.068") |
| *5F-C | Reperfusion 054 | Penumbra | 1.37 (0.054") | 6F, 2.00 (0.080") |
| *4F | DAC 044 | Stryker NV | 1.10 (0.044") | 4.3F, 1.45 (0.058") |
| 4F-B | Reperfusion 041 | Penumbra | 1.04 (0.041") | 4.1F, 1.37 (0.054") |
| 4F-C | Chaperone Inner | Stryker NV | 1.00 (0.041") | 4.1F 1.33 (0.052") |
| *3F | DAC 038 | Stryker NV | 0.89 (0.036") | 3.9F, 1.30 (0.052") |
| 2F-B | Excelsior SL-27 | Stryker NV | 0.69 (0.027") | 2.7F, 0.90 (0.036") |
| 2F | Excelsior SL-10 | Stryker NV | 0.57 (0.022") | 1.7F, 0.57 (0.022") |
| MW | Transend EX-14 | Stryker NV | Not applicable (microwire) | 1.1F, 0.36 (0.014") |

Supplementary Table 4. Coaxial catheter delivery system. Combinations assessed for access and deployment of stentrodie into the superior sagittal sinus. Catheters with asterisks identify the catheter utilised as delivery catheter for the stentrodie within the coaxial combination.

| Sheath | Guide catheter | Distal access catheter | Microcatheter | Microwire |
|---------------|-----------------------|-------------------------------|----------------------|------------------|
| 6F | 6F* | 4F-B | 2F | MW |
| 6F | 5F* | 4F-C | 2F | MW |
| 6F | 5F-B* | 4F-C | 2F | MW |
| 6F | 6F | 4F* | 2F-B | MW |
| 6F | 5F | 4F-B* | 2F | MW |
| 6F | 5F | 4F-C* | 2F | MW |

Supplementary Table 5. Ex vivo superior sagittal sinus internal lumen areas. Median, interquartile range (IQR) and range (minimum to maximum) of lumen areas from animals implanted with a stent within the superior sagittal sinus for up to 190 days assessed using synchrotron x-ray imaging. Slices were taken from synchrotron images separated by 1 mm from the proximal to distal tip of the stent. The control animal did not have a device implanted.

| Subset (Number of animals) | Days Implanted | Number of slices | Lumen Area (mm ²) | |
|----------------------------------|-------------------|---------------------|-------------------------------|--------------------|
| | | | Median [IQR] | Range (min-max) |
| Control (1) | n/a | 20 | 5.59 [5.51, 6.13] | 5.06-6.31 |
| 0-1 days (2) | 0 | 20 | 5.64 [4.95, 6.19] | 3.71-6.68 |
| | 1 | 25 | 5.49 [4.85, 5.86] | 2.72-6.21 |
| 0-2 weeks (2) | 9 | 29 | 3.36 [3.13, 3.78] | 2.75-4.68 |
| | 14 | 20 | 4.02 [3.84, 4.14] | 3.05-4.29 |
| 2-4 weeks (1) | 27 | 20 | 3.02 [2.91, 3.93] | 2.11-5.95 |
| 4-8 weeks (2) | 34 | 22 | 3.47 [3.22, 3.67] | 3.04-3.84 |
| | 56 | 24 | 3.79 [2.64, 4.19] | 2.11-5.52 |
| 8-12 weeks (2) | 77 | 22 | 2.60 [1.82, 3.58] | 1.58-4.62 |
| | 83 | 18 | 1.86 [1.80, 2.11] | 1.70-2.68 |
| 12-16 weeks (3) | 91 | 20 | 3.49 [3.38, 3.59] | 2.96-3.79 |
| | 97 | 20 | 3.59 [3.35, 4.07] | 2.78-4.38 |
| | 98 | 23 | 4.42 [4.04, 4.68] | 3.78-4.79 |
| 16-20 weeks (3) | 113 | 26 | 4.42 [4.09, 4.60] | 3.03-5.67 |
| | 124 | 20 | 2.88 [2.68, 3.02] | 1.90-3.79 |
| | 124 | 20 | 3.45 [3.26, 3.59] | 3.14-4.00 |
| 20-28 weeks (4) | 153 | 20 | 5.35 [5.25, 5.59] | 4.82-6.03 |
| | 182 | 18 | 3.70 [3.25, 4.33] | 2.19-5.72 |
| | 183 | 20 | 4.99 [4.81, 5.10] | 4.49-5.37 |
| | 190 | 20 | 3.59 [3.29, 3.82] | 2.59-4.20 |

Supplementary Table 6. Maximum bandwidth over duration of implantation. Maximum average bandwidth, standard deviation and range of recorded signals from animals implanted with a stentrod electrode within the superior sagittal sinus overlying the motor cortex for up to 190 days. Each sample (single electrode per recording-day) had a minimum of 20 epochs, with an average of 74.1 ± 54 epochs (mean \pm SD, range [21-337] epochs).

| Implant Duration (days) | Number of Animals | Number of Samples | Maximum Bandwidth (Hz) | |
|-------------------------|-------------------|-------------------|------------------------|-----------------|
| | | | Mean \pm SD | Range (min-max) |
| 0-2 weeks | 10 | 132 | 197.4 \pm 42.0 | 120-406 |
| 2-4 weeks | 8 | 75 | 183.9 \pm 34.6 | 120-320 |
| 4-8 weeks | 7 | 82 | 180.7 \pm 35.0 | 120-281 |
| 8-12 weeks | 3 | 55 | 210.2 \pm 26.7 | 155-300 |
| 12-16 weeks | 3 | 34 | 188.0 \pm 38.0 | 120-295 |
| 16-20 weeks | 1 | 18 | 196.7 \pm 36.0 | 146-290 |
| 20-28 weeks | 2 | 8 | 194.4 \pm 20.8 | 178-245 |

Supplementary Note 1

Mapping cerebral veins and cortical surface

Methods

Subjects. Consent from the Royal Melbourne Hospital (Victoria, Australia), Human Research and Ethics Committee (HREC) was obtained to query the imaging archive and perform retrospective analysis of de-identified MRI studies. Between June 2011 and September 2013, 60 contrast enhanced MRI studies were collected. Of those, ten studies were excluded from analysis due to poor image quality (movement artifact) and/or ineffective automated analysis. Records were de-identified and an anonymous code was created to facilitate blinded assessment of MRIs.

Observer error. To quantify intra-observer error, vein diameter measurements were repeated (TO) in 30 subjects, using an externally derived, random and blinded code. To quantify inter-observer error in diameter measurements, a second observer (neuroradiologist, EL) conducted a repeat set of blinded diameter measurements on a random sample of ten patients.

Vein intersection angles. To assess the intersection angle of tributary superficial vein entry into superior sagittal sinus (SSS), the fiducial points of each subject were imported into MATLAB (R2014a, v8.3.0.532, Natick, Massachusetts: The MathWorks Inc., 2010) and visualized using a 3D scatter plot. Vectors were calculated using the difference between Cartesian coordinates of fiducial points neighbouring the intersection of the SSS and all relevant cortical veins. The points used were verified by visual inspection. Angles were then measured as the arccosine of the SSS vector (\vec{v}_{SSS}) and secondary vein vector (\vec{v}_{SV}):

$$\theta = \arccos \left(\frac{\vec{v}_{SSS} \cdot \vec{v}_{SV}}{\|\vec{v}_{SSS}\| * \|\vec{v}_{SV}\|} \right) * \frac{180}{\pi} \quad (1)$$

Data analysis. To investigate both the inter- and intra-observer reliability when measuring vein diameters, the magnitude of agreement was estimated using Intraclass Correlation Coefficients (ICC)¹ and further validated using Lin's Concordance Correlation Coefficients (CCC)². The magnitude of agreement was assessed using the following scale: 0.00 = poor, 0.00 – 0.20 = slight, 0.21 – 0.40 = fair, 0.41 – 0.60 = moderate, 0.61 – 0.80 = substantial, and 0.81 – 1.00 = almost perfect agreement³. In addition, a reduced major axis regression analysis was conducted. A subgroup analysis of proximal regions of veins (the proximal 20 mm of diameter measurements) was performed following observation of increased anatomical irregularity.

Supplementary Note 2

Stentrode delivery

Methods:

Delivery force testing. A sheep vasculature model was developed to mimic the venous anatomical device insertion pathway from external jugular vein to SSS, by routing a 2.0 mm internal diameter catheter around a sheep skull (Supplementary Fig. 4a). As solitaire stents (Solitaire SAB, Covidien, CA, USA) detach with a force of 4-6 N⁴, internal friction forces were measured along the anatomical pathway as stentodes were pushed through various delivery catheters (see Supplementary Fig. 4b) with a Mark-10 Series force gauge (M5-05 260F, IDM Instruments, NY, USA).

Compression Tests. To ensure that stents would retain their superelastic properties and mechanical integrity following attachment of electrodes and weaving of electrode lead wires, compression tests were conducted. Stentodes with six, seven or eight electrodes were mounted to long (SAB 3-30, 44.8 mm length, 3mm diameter, Covidien, CA, USA) and short (SAB 3-20, 31.1 mm length, 3 mm diameter) stents. Devices were mounted to a micromanipulator controlled base plate with the electrodes facing up. The stents were compressed along the midline at $100 \pm 10 \mu\text{m}$ intervals with a 12.7 mm diameter flat head attachment, connected to a force gauge at a connection diameter of less than 1 mm. Stress (g/cm^2) was calculated as the force resulting from compression of the area of the 12.7 mm diameter flat head attachment, with strain evaluated as the compressed distance divided by the nominal stent diameter⁵.

Results:

Delivery force testing. While no stentodes required forces greater than 4 N (limit for stent fracture) for delivery, an eight-electrode stentode required a maximal delivery force of 2.05 ± 0.17 N (mean \pm SD, $n = 3$) to be deployed through a 0.89 mm internal diameter (ID) catheter (DAC038, Stryker NV, CA, USA) and was associated with electrode detachment. When delivered through a catheter with an ID of 1.1 mm (DAC044, Stryker, NV, CA, USA) a maximum force of 0.67 ± 0.14 N (mean \pm SD, $n = 9$) was observed, with no electrode detachment. The 1.1 mm ID catheter was therefore selected as the delivery catheter.

Compression Tests. Both short and long stentodes with six to eight electrodes were observed to maintain the superelastic properties of the stent, returning to the nominal diameter (3 mm) post compression. There were negligible force differences when compressing a stentode to 1 mm (33% nominal diameter) between seven and eight electrodes using a long stent, and six and seven electrodes using the short stent. A negligible force differential was also observed between the short and long stents with seven electrodes as a function of length (57.7 ± 5.4 g for the short, 31.1 mm stent and 52.28 ± 8.3 g for the long, 44.8 mm stent).

Supplementary Note 3

Vessel wall integration

Methods

Electrochemical impedance spectroscopy. Impedance and phase angle measurements were used to exclude electrodes that were short circuited to the stent wire through leakage of electrolytic fluid into the connector block (Supplementary Fig. 6). Electrochemical Impedance Spectroscopy (EIS) of stent-mounted electrodes immersed in saline were observed to exhibit a response characteristic of metal electrodes⁹, appearing like a low pass filter with a peak resistance frequency of 200 kHz and respective access resistance of $816 \pm 15 \Omega$ (mean \pm SD, n = 39 electrodes)⁷. To identify electrodes that were no longer insulated from the stent, EIS of bare metal stents immersed in saline was performed (Supplementary Fig. 6). These devices exhibited a decreased peak resistance frequency of 15.9 kHz and corresponding access resistance of $620 \pm 27 \Omega$ (mean \pm SD, n = 12 stents). Immediately following implantation, seven electrodes were observed to be short circuited to the stent wire. These electrodes exhibited a significant decrease in 10 kHz impedance magnitude compared with viable electrodes (short circuited electrodes, $659 \pm 113 \Omega$, mean \pm SD, n = 7; viable electrodes $2662 \pm 486 \Omega$, mean \pm SD, n = 28). As such, electrodes with a measured 10 kHz impedance magnitude less than 1 k Ω were excluded from signal analysis.

Supplementary Note 4

Vessel wall integration

Methods

Circuit model. A simple equivalent circuit model (Supplementary Fig. 7) was developed to model impedance changes following implantation. The model comprised of three components: a solution resistance, an electrode-tissue interface, and a tissue impedance. The solution impedance (R_S) represents the circuit access impedance, including the cables and wires from the potentiostat to the working and reference electrodes. The electrode-tissue interface was modelled by a Faradaic charge transfer resistance (R_E) and a double-layer constant phase element (CPE_E)⁶. The non-Faradaic impedance (constant phase element impedance) is given by the empirical relation

$$Z_{CPE} = \frac{1}{Q(j\omega)^\alpha} \quad (2)$$

where Q is the impedance magnitude and α is the exponent term of the CPE that represents inhomogeneity's in the electrode surface. When $\alpha = 1$, the CPE acts like a purely capacitive element and when $\alpha = 0$, like a purely resistive element. Decreases in α have been reported to infer protein adsorption occurring at the electrode surface^{7,8}. The tissue resistance was included to model the impedance fluid (R_T , set to zero in saline), and capacitance of cell membranes and encapsulating tissue (C_S) present between the reference and working electrodes⁷. The model was fitted to imported *in vivo* measurements with Gamry Echem Analyst (6.2.2, Gamry Instruments, USA) using a simplex, least-squares method.

Supplementary Note 5

Vascular Electrocardiography

Methods:

Chewing muscle artifact. Chewing artifacts from recordings were identified by first notch filtering (50 Hz and harmonics) and then band pass filtering (200 - 800 Hz) with fourth order zero-phase Butterworth filters. The amplitude envelope of each signal was extracted by applying a Hilbert transform on the filtered and standardized signal. The width of each envelope was estimated as the distance between the points on either side of the artifact peak, where the envelope intercepted a root mean square (RMS) value of the recording. Peaks were then verified by a post-hoc visual inspection. Signal baseline was defined as a period preceding the artifact of the same envelope width. We calculated the ratio of the RMS of each artifact identified, to that of the baseline, for each animal. The signal used for the artifact-to-baseline ratio was notch filtered (50 Hz and harmonics) and band pass filtered (4 - 1000 Hz) using fourth order zero-phase Butterworth filters. A tukey-corrected one-way ANOVA was performed to compare the artifact to baseline ratio between the three arrays.

Supplementary Note 6

Vascular Electrocochography

Methods:

Stentrode position co-registration. MRI scans of brains were performed on all sheep prior to implant with stentrodes. At least one week post angiography, non-contrast CT brains (Somatom, 128 slice, Siemens, Erlangen, Germany) were performed under similar general anesthesia conditions as for MRI acquisition. CT images were reconstructed with 0.6 mm slices, and co-registered to pre-implantation MRI scans using ANTS¹⁰. For the purpose of graphic representation, one high resolution Corriedale sheep 7T MRI brain scan was acquired (Magnetom 7T, Siemens, Germany), co-registered to 1.5T MRI scans and segmented to form a 3D cortical surface representation using ITK-SNAP¹¹.

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