A hierarchical anatomical framework and workflow for organizing stereotactic encephalography in epilepsy

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Abstract

Stereotactic electroencephalography (SEEG) is an increasingly utilized method for invasive monitoring in patients with medically intractable epilepsy. Yet, the lack of standardization for labeling electrodes hinders communication among clinicians. A rational clustering of contacts based on anatomy rather than arbitrary physical leads may help clinical neurophysiologists interpret seizure networks. We identified SEEG electrodes on post-implant CTs and registered them to preoperative MRIs segmented according to an anatomical atlas. Individual contacts were automatically assigned to anatomical areas independent of lead. These contacts were then organized using a hierarchical anatomical schema for display and interpretation. Bipolar-referenced signal cross-correlations were used to compare the similarity of grouped signals within a conventional montage versus this anatomical montage. As a result, we developed a hierarchical organization for SEEG contacts using well-accepted, free software that is based solely on their post-implant anatomical location. When applied to three example SEEG cases for epilepsy, clusters of contacts that were anatomically related collapsed into standardized groups. Qualitatively, seizure events organized using this framework were better visually clustered compared to conventional schemes. Quantitatively, signals grouped by anatomical region were more similar to each other than electrode-based groups as measured by Pearson correlation. Further, we uploaded visualizations of SEEG reconstructions into the electronic medical record, rendering them durably useful given the interpretable electrode labels. In conclusion, we demonstrate a standardized, anatomically grounded approach to the organization of SEEG neuroimaging and electrophysiology data that may enable improved communication among and across surgical epilepsy teams and promote a clearer view of individual seizure networks.
INTRODUCTION

Of the approximately 50 million people with epilepsy worldwide, around one-third of cases are resistant to medication (GBD 2016 Brain and Other CNS Cancer Collaborators, 2019; Kwan & Brodie, 2000; Picot et al., 2008; Sander, 1993). These patients should be evaluated for epilepsy surgery if amenable, which can include resection or ablation of the seizure focus, or neuromodulation of the seizure network. If they undergo one of these operations, the degree of postoperative seizure control is heavily dependent on identification and disablement of the epileptogenic zone (Englot et al., 2012, 2013; Jobst & Cascino, 2015).

Noninvasive diagnostic measures for characterizing seizure networks can include magnetic resonance imaging (MRI), surface electroencephalography (EEG), positron emission tomography (PET), magnetoencephalography (MEG), and neuropsychological evaluations. However, patients may elect to undergo invasive monitoring if clinical data do not converge on a clear seizure source to address surgically (Diehl & Luders, 2000; Sarkanen, 2015). The two primary methods for intracranial recordings are via stereotactic(stereo)-EEG (SEEG) depth electrodes and subdural electrode grids and strips. The advantages and disadvantages of each have been extensively studied, reported, and reviewed (Podkorytova et al., 2016). Though the factors influencing the choice between these two procedures are complex, it is now generally well-accepted that SEEG entails fewer complications while enabling access to more brain regions for exploration (Mullin et al., 2016; Podkorytova et al., 2016; Taussig et al., 2020).

However, whereas subdural grids have the advantage of a regular arrangement of electrodes such that the relationships of signals across contacts have an intuitive spatial order, SEEG depth electrode placement can be highly variable in trajectory, contact geometry, and lead spacing. To mitigate this, some groups have advocated for the use of orthogonal lead placements and “typical” trajectories (Bourdillon et al., 2018; Faraji et al., 2020; Khoo et al., 2020). Others, meanwhile, have created labeling algorithms to standardize SEEG nomenclature based upon lead trajectories (Stone et al., 2020). Unfortunately, the former approach may constrain the use of SEEG in a flexible and patient-specific manner, while the proposed labeling schemes are rather complex and unintuitive, limiting widespread adoption. Furthermore, these approaches tend to ignore the problem of organizing the display of signals in a manner that is sufficiently consistent across cases to allow the development of some visual intuition for interpretation, yet flexible enough to enable application across widely varying implant strategies.

To address these limitations, we propose a framework that is built up from the “ground truth” of brain anatomy and abstracted from the arbitrary details of implant technology. In other words, rather than treating the lead that carries electrodes as the basic unit of neurophysiology, as is currently done with existing nomenclatures and typical montages, we consider individual contacts independently of the leads that support them and assign contact labels and relative organization based upon a rational, hierarchical anatomical schema.

We demonstrate this approach by building a pipeline for organizing SEEG imaging and electrophysiological data using well-accepted, free neuroimaging tools and clinically indicated images. By adapting a standard atlas, our approach applies hierarchical labeling of SEEG contacts abstracted from the arbitrary constraints of the physical leads (Jung et al., 2021; Reuley et al., 2017). As a simple example of the flavor of this approach, one can appreciate that the deeper (more distal) contacts on a series of depth leads targeting the medial temporal lobe are likely more electrographically similar to each other than with the more proximal contacts that target the lateral temporal lobe. Thus, grouping contacts as medial versus lateral may be preferred over grouping them according to the leads on which they reside. Further, those lateral contacts may be best viewed as clustered according to gyrus as well as anterior–posterior position, especially when SEEG lead density is high. This general approach can be combined with existing brain parcellation software to cluster and label contacts based on patient-specific anatomy down to the gyrus, sulcus, or nucleus (Desikan et al., 2006; Destrieux et al., 2010). In addition, we argue that exporting final products of this parcellation, incorporating broadly understood anatomical labels, to the electronic medical record (EMR) can improve communication among the clinical team by allowing all individuals to view the results of this approach without the need for familiarity with specialized software used to create those results.

MATERIALS AND METHODS

The minimum subject-specific image sequences needed include preoperative T1-weighted MRI and postoperative computed tomography (CT) of the brain, which are both already obtained for the routine clinical course (Figure 1). Though not strictly required, the surgical plan of electrode trajectories is extremely helpful for identifying electrodes on imaging, particularly in complex explorations. While we generate and illustrate each component using common and accessible research and clinical software, this general pipeline is well-established and the precise tools used to achieve any step may be adapted based on institutional preference.

During data exportation and prior to any processing, image sequences were anonymized to maintain strict patient privacy in accordance with the Health Insurance Portability and Accountability Act (HIPAA) and the local Institutional Review Board (IRB #217972).

CT/MRI registration

In order to ultimately associate contacts, which can be visualized using high-resolution post-implantation CT, with an anatomical location, they must be transformed into the same space as the reference preoperative
MRI. We used a step-wise process starting within the surgical planning software used to draft depth electrode trajectories (Waypoint Navigator, v4.6, FHC). First, we registered the preoperative MRI to a preoperative CT angiograph (CTA) via an automatic nonrigid algorithm, then registered the postoperative CT to the preoperative CTA, transitively transforming the preoperative MRI to postoperative CT space.

2.2 Brain parcellation

Our labeling scheme relies on automatic segmentation of cortical and subcortical regions of interest for each patient. We implemented the recon_all function in FreeSurfer v7.1.0 (Athinoula A. Martinos Center for Biomedical Imaging) to accomplish this step. Importantly, the Desikan-Killiany (DK) atlas incorporated in FreeSurfer is already roughly hierarchically organized and can therefore be easily adapted generally to compile the final tree of labels. Modifications to the DK atlas, namely to segment amygdaloid and hippocampal subfields, thalamic nuclei, and insular gyri, were made using the Destreux cortical atlas in FreeSurfer and other incorporated atlases (Destrieux et al., 2010; Fischl et al., 2004; Iglesias et al., 2015, 2016, 2018; Saygin et al., 2017).

2.3 Contact segmentation

Each depth electrode is assigned a unique label, based on the electrode target. Each electrode contact along the depth electrode is assigned a number based on physical location along the lead, usually ascending deep-to-superficial. Indeed, these labels are typically used for all further communication and conceptualization of neurophysiological data. Further, these labels are also usually used by the clinical electrophysiology software for organizing EEG montages, which are subsequently interpreted by a neurologist.

Electrodes seen on postoperative CT can be identified using the intended trajectories from the surgical plan. We then used 3DSlicer (v4.11, Brigham and Women’s Hospital) markups to reconstruct models of each electrode based on specifications from the electrode manufacturer (MICRODEEP Depth Electrodes, DIXI Medical), giving each contact name a coordinate in the CT/MR/Parcellation space (Fedorov et al., 2012). Using the Python interface in 3DSlicer, we automatically generate a list of each contact with its coordinates and location within the segmented brain, which can be grouped hierarchically based on anatomy.

2.4 Neurophysiological montages

Signals were lowpass filtered using a second-order Butterworth filter (cutoff frequency = 200 Hz). For visualization, signals were displayed as a montage using a bipolar referencing scheme, subtracting the adjacent superficial signal from each contact, as is common in clinical practice. Signals were manually inspected and those with significant artifact were excluded from the analysis. Of note, contacts located in white matter but that were within 2 mm of a gray matter segment.

**FIGURE 1** General schematic for generating anatomical electrode labels. The segmented T1-weighted MR is used to bridge electrodes seen on postoperative CT to patient anatomy-space. The final output of this imaging pipeline is a re-organized hierarchical spreadsheet of contacts that associates preoperative labels with a new abstracted one.
| FreeSurfer label | Level 1: lobe | Level 2: region | Level 3: gyrus/nucleus | Location | Coordinate preference |
|-----------------|--------------|----------------|------------------------|----------|-----------------------|
| Lateral-nucleus | Temporal     | Medial         | Amygdala: lateral nucleus | Lateral nucleus | ap                    |
| Basal-nucleus   | Temporal     | Medial         | Amygdala: basal nucleus  | Basal nucleus | ap                    |
| Central-nucleus | Temporal     | Medial         | Amygdala: central nucleus | Central nucleus | ap                    |
| Medial-nucleus  | Temporal     | Medial         | Amygdala: med. nucleus  | Medial nucleus | ap                    |
| Cortical-nucleus| Temporal     | Medial         | Amygdala: cortical nucleus | Cortical nucleus | ap                  |
| Accessory-basal-nucleus | Temporal | Medial | Amygdala: accessory basal nucleus | Accessory basal nucleus | ap |
| Corticoamygdaloid-transition | Temporal | Medial | Amygdala: corticoamygdaloid transition | Corticoamygdaloid transition | ap |
| Anterior-amyg. area-AAA | Temporal | Medial | Amygdala: anterior area | Anterior amygd. area | ap |
| Paralaminar-nucleus | Temporal | Medial | Amygdala: paralaminar nucleus | Paralaminar nucleus | ap |
| Amygdala | Temporal     | Medial         | Hippocampus: amygdala   | Amygdaloid unknown | ap |
| Parasubiculum  | Temporal     | Medial         | Hippocampus: parasubiculum | Parasubiculum | ap |
| Presubiculum   | Temporal     | Medial         | Hippocampus: presubiculum | Presubiculum | ap |
| Subiculum      | Temporal     | Medial         | Hippocampus: subiculum  | Subiculum | ap |
| CA1            | Temporal     | Medial         | Hippocampus: CA1        | CA1      | ap |
| CA3            | Temporal     | Medial         | Hippocampus: CA3        | CA3      | ap |
| CA4            | Temporal     | Medial         | Hippocampus: CA4        | CA4      | ap |
| GC-DG          | Temporal     | Medial         | Hippocampus: dentate gyrus | Dentate gyrus | ap |
| HATA           | Temporal     | Medial         | Hippocampus: HATA       | Hippocampal amygdala transition area | ap |
| Fimbria        | Temporal     | Medial         | Hippocampus: fimbria    | Fimbria  | ap |
| Molecular_layer_HP | Temporal | Medial | Hippocampus: molecular layer | Hippocampal molecular layer | ap |
| Hippocampal_fissure | Temporal | Medial | Hippocampus: fissure | Hippocampal fissure | ap |
| HP_tail        | Temporal     | Medial         | Hippocampus: tail       | Hippocampal tail | ap |
| Hippocampus    | Temporal     | Medial         | Hippocampus             | Hippocampal unknown | ap |
| Entorhinal     | Temporal     | Medial         | Entorhinal cortex       | Entorhinal cortex | ap |
| Parahippocampal | Temporal       | Medial | Parahippocampal gyrus | Parahippocampal gyrus | ap |
| Temporalpole   | Temporal     | Medial         | Temporal pole           | Temporal pole | ap |
| Fusiform       | Temporal     | Medial         | Fusiform gyrus          | Fusiform gyrus | ap |
| Superiortemporal | Temporal | Lateral | Superior temporal gyrus | Superior temporal gyrus | ap |
| Middletemporal | Temporal     | Lateral | Middle temporal gyrus | Middle temporal gyrus | ap |
| Inferiortemporal | Temporal | Lateral | Inferior temporal gyrus | Inferior temporal gyrus | ap |
| Transversetemporal | Temporal | Lateral | Transverse temporal cortex | Transverse temporal cortex | ap |
| Frontalpole    | Frontal      | Anterior       | Frontal pole            | Frontal pole | ap |
| Superiorfrontal | Frontal | Superior | Superior frontal gyrus | Superior frontal gyrus | ap |
| Rostralmiddlefrontal | Frontal | Middle | Middle frontal gyrus | Rostral middle frontal gyrus | ap |
| Caudalmiddlefrontal | Frontal | Middle | Middle frontal gyrus | Caudal middle frontal gyrus | ap |
| Parsopercularis | Frontal | Inferior | Inferior frontal gyrus | Pars opercularis | ap |
| Parstriangularis | Frontal | Inferior | Inferior frontal gyrus | Pars triangularis | ap |
| Parsorbitalis  | Frontal      | Inferior       | Inferior frontal gyrus  | Pars orbitalis | ap |
| Medialorbitofrontal | Frontal | Orbitofrontal | Orbitofrontal cortex | Medial orbitofrontal cortex | ap |
| Lateralorbitofrontal | Frontal | Orbitofrontal | Orbitofrontal cortex | Lateral orbitofrontal cortex | ap |

(Continues)
| FreeSurfer label | Level 1: lobe | Level 2: region | Level 3: gyrus/nucleus | Location | Coordinate preference |
|-----------------|--------------|----------------|------------------------|----------|----------------------|
| Paracentral     | Frontal      | Central        | Paracentral lobule     | Paracentral lobule | ap        |
| Precentral      | Frontal      | Central        | Precentral gyrus       | Precentral gyrus  | si        |
| Insular_short   | Insula       | Short          | Insula: short gyri     | Short insular gyri| si        |
| Ins_lg_and_S_cent_ins | Insula     | Long           | Insula: long gyri      | Long insular gyri | si        |
| Circular Insula_ant | Insula      | Circular       | Insula: anterior circular sulcus | Anterior circular insular sulcus | si        |
| Circular Insula_inf | Insula      | Circular       | Insula: inferior circular sulcus | Inferior circular insular sulcus | ap        |
| Insula_sup      | Insula       | Other          | Insula                 | Insular unknown  | ap        |
| Postcentral     | Parietal     | Central        | Postcentral gyrus      | Postcentral gyrus | si        |
| Superiorparietal | Parietal     | Superior       | Superior parietal cortex | Superior parietal cortex | ap        |
| Inferiorparietal | Parietal     | Inferior       | Inferior parietal cortex | Inferior parietal cortex | ap        |
| Supramarginal   | Parietal     | Inferior       | Supramarginal gyrus    | Supramarginal gyrus | ap        |
| Precuneus       | Parietal     | Medial         | Precuneus cortex       | Precuneus cortex | ap        |
| Rostralantiercingulate | Cingulate | Anterior      | Anterior cingulate cortex | Rostral anterior cingulate cortex | ap        |
| Caudalantiercingulate | Cingulate | Anterior      | Anterior cingulate cortex | Caudal anterior cingulate cortex | ap        |
| Posteriorcingulate | Cingulate   | Posterior      | Posterior cingulate cortex | Posterior cingulate cortex | ap        |
| Isthmuscingulate | Cingulate    | Inferior      | Isthmus of cingulate gyrus | Isthmus of cingulate gyrus | ap        |
| Corpuscallosum  | Cingulate    | Inferior      | Corpus callosum        | Corpus callosum  | ap        |
| Cuneus          | Occipital    | Medial         | Cuneus cortex          | Cuneus cortex    | ap        |
| Pericalcarine   | Occipital    | Medial         | Pericalcarine cortex   | Pericalcarine cortex | ap        |
| Lingual         | Occipital    | Medial         | Lingual cyrus          | Lingual cyrus    | ap        |
| Lateraloccipital | Occipital    | Lateral       | Lateral occipital cortex | Lateral occipital cortex | ap        |
| AV              | Thalamus     | Anterior       | Thalamus:AV nucleus    | Anteroventral nucleus | ap        |
| LD              | Thalamus     | Lateral        | Thalamus:LD nucleus    | Laterodorsal nucleus | ap        |
| LP              | Thalamus     | Lateral        | Thalamus:LP nucleus    | Lateral posterior nucleus | ap        |
| VA              | Thalamus     | Ventral        | Thalamus:VA nucleus    | Ventral anterior nucleus | ap        |
| VAmc            | Thalamus     | Ventral        | Thalamus:VA magnocellular nucleus | Ventral anterior magnocellular nucleus | ap        |
| Vla             | Thalamus     | Ventral        | Thalamus:VLa nucleus   | Ventral lateral anterior nucleus | ap        |
| VLP             | Thalamus     | Ventral        | Thalamus:VLP nucleus   | Ventral lateral posterior nucleus | ap        |
| VM              | Thalamus     | Ventral        | Thalamus:VM nucleus    | Ventromedial nucleus | ap        |
| CeM             | Thalamus     | Intralaminar   | Thalamus:CeM nucleus   | Central medial nucleus | ap        |
| CL              | Thalamus     | Intralaminar   | Thalamus:CL nucleus    | Central lateral nucleus | ap        |
| Pc              | Thalamus     | Intralaminar   | Thalamus:Pc nucleus    | Paracentral nucleus | ap        |
| CM              | Thalamus     | Intralaminar   | Thalamus:CM nucleus    | Centromedial nucleus | ap        |
| Pf              | Thalamus     | Intralaminar   | Thalamus:Pf nucleus    | Parafascicular nucleus | ap        |
| Pt              | Thalamus     | Medial         | Thalamus:Pt nucleus    | Paratenial nucleus | ap        |
| MV-re           | Thalamus     | Medial         | Thalamus:reuniens nucleus | Reuniens nucleus | ap        |
| MDm             | Thalamus     | Medial         | Thalamus:MDm nucleus   | Mediodorsal medial magnocellular nucleus | ap        |
were included in that segment but were marked as exceptions. Remaining white matter contacts were positioned at the bottom of the anatomical montages. Clinical EEG interpretations were reviewed for contacts or electrode regions (e.g., deep or superficial) that were noted to be involved in a particular seizure.

Signal similarity was assessed using the average Pearson product–moment correlation coefficients ($r$) for contacts grouped by anatomical regions and by physical lead. In order to mitigate the effects of co-dependencies between signals caused by bipolar referencing, an average "group signal" was calculated for every anatomical segment and physical electrode. Then, each signal used to obtain the mean signal was correlated to it, resulting in a distribution of $r$ values based on each signal under the anatomical and conventional schemes. An independent two-tailed $t$-test was used to assess for differences in mean Pearson correlations within fundamental units of the anatomical (segmented regions) versus conventional (depth electrodes) montages.

### RESULTS

#### 3.1 Hierarchical framework

We first constructed a hierarchical classification of brain regions based upon the labels extracted from an adapted DK human brain atlas (Table 1). For cortical regions, the hierarchy was built up from gyrus to lobe to hemisphere (Figure 2). Priority was given for sites within a single gyrus assigned anterior before posterior, as the principal axis for several frequently sampled regions (e.g., hippocampus, superior/middle/inferior temporal gyri) is most parallel to that axis. Exceptions were made for the few gyri such as the motor and sensory cortices whose major axes run inferiorly, in which case priority was given to superior sites. For subcortical structures, the hierarchy was built up from nucleus to nuclear group to hemisphere, with the same Cartesian preferences for location within a nucleus. An implicit "zeroth" level denotes the hemisphere of the contact coordinates.

#### 3.2 Illustrative cases

The hierarchical labeling scheme was then applied to three patients with medically intractable epilepsy who underwent SEEG explorations at our institution. Characterization of each subject and their epilepsies is outlined in Table 2. We registered each preoperative T1 MRI to a high-resolution postoperative CT. After cortical segmentation, all contacts were then associated with their preoperative label and modeled in 3DSlicer. The coordinates of each contact were then used to associate each contact with a region of interest as defined by the patient-specific brain parcellation. Our framework was applied to this list to automatically reorganize the list of contacts from preoperative physical leads to a spreadsheet organized by an anatomically based hierarchy. The relabeled contacts were applied and overlayed on the CT-MRI registrations for end-user visualization. At this point, leads are associated with known anatomy and consequently can be generally understood. Reconstructions may therefore be uploaded to the standard picture archiving and communication systems (PACS) as a permanent part of the patient's EMR to aid in all future clinical assessments.
To more fully illustrate the clinical utility of this framework, we created montages capturing a seizure from three SEEG cases. By design, clusters of electrodes that were anatomically related collapsed into standardized groups. Consequently, contacts noted to be clinically relevant often cluster, facilitating interpretation of the seizure network. For Subject 1 (Figure 3), the deep contacts of electrodes targeting the amygdala and hippocampus (A-AMY, B-PHIP, C-MHIP) were consistently noted in clinical EEG interpretations of captured seizures, and expectedly aggregated as medial temporal lobe contacts when anatomically organized. Likewise, for Subject 2 (Figure 4), deep contacts targeting the medial temporal lobe clustered together (L-AMYG, L-HIPB, L-HIPH) along with deep contacts on insular (L-PINS) and opercular (L-OPER) electrodes. By segmenting out white matter electrodes and relegating them to the bottom of the montage, the temporal onset and likely spread to the frontal lobe was visually more apparent. Subject 3, who had multiple MRI
abnormalities but no scalp correlate to her brief asymmetric tonic seizures, was implanted with broad bilateral coverage across multiple lobes that were notably fragmented on the traditional montage (Figure 5). When translated to the anatomical montage, the frontal, temporal, parietal, and thalamic electrodes were discriminated, with clinically noted seizure nodes emerging along either side of the central sulcus, within the Perisylvian polymicrogyria. Both of these nodes combined deep contacts from electrodes (L-PAR, L-INSU, L-PSYL) that were disparate on the conventional clinical montage. These findings for Subject 3 were used to infer that the electrodes were within the network of the seizure (i.e., the epileptogenic region) but not the seizure onset zone.

For each of the three processed seizure recordings, the distribution of signal correlations of contacts within the same electrode and the same anatomical region with the average signal within each were compared (Figure 6). The neurophysiologic signals, which were bipolar referenced by electrode, were more highly correlated to the group-averaged signal in the anatomical montage than in the traditional lead-based montage. This trend was statistically significant for all three subjects (p < .01; two-tailed t-test for differences in means) as well as for the aggregated comparisons (p < .0001; two-tailed t-test).

4 | DISCUSSION

We offer a hierarchical labeling of SEEG contacts that is based on precise postoperative location of depth electrode contact within patient-specific anatomy. There have been multiple tools and pipelines developed for localization of depth electrodes in the context of SEEG using some or all of the same software reported here (Davis et al., 2021; Medina Villalon et al., 2018; Narizzano et al., 2017; Princich et al., 2013; Qin et al., 2017; Taylor et al., 2021). Each has its own advantages, such as speed and efficiency, extent of clinical validation, and detailed considerations such as accounting for electrode curve. Yet in addition to limited adoption, previously reported methods persistently remain constrained to the initial contact labels extended from physical leads. Therefore, they fail to leverage the potential to reorganize electrodes anatomically. The primary advantage of our approach is that it begets an intuitive shift in perspective from preoperative target-centered labels to anatomically-based hierarchical ones.

Further, our schema is similar to the clinical approach for interpreting seizures on scalp (Tanaka et al., 2018) and subdural EEG studies (Blume et al., 2001; Devinsky et al., 1989). For those investigations, there is an anatomic spatial arrangement used to evaluate seizures in context of their physiologic field. The spread of discharges
FIGURE 4  Demonstration of the anatomical framework for a subject suffering from seizures with temporal lobe onset and secondary generalization from a complex bilateral SEEG case (Subject 2)*. There were three left MTL electrodes targeting the (a) hippocampal head, (b) hippocampal body, and (c) amygdala. Each was comprised of (i) a deep segment within the amygdala or hippocampus that was involved in the clinical seizure, (ii) an intermediate segment of white matter contacts, and (iii) a superficial group of contacts within the middle temporal gyrus. (d) A 3D model of the electrodes in panels a–c sampling the left temporal lobe further illustrates the spatial relationship of the medial versus lateral contacts. (e) In the electrophysiological montages, a clinical seizure begins before the 1-min mark of this 2 min section of recording. There were multiple electrode regions involved in the onset and generalization of the seizure, spanning amygdaloid, hippocampal, cingulate, and insular electrodes. (f) Deep contacts from electrodes targeting the MTL were clustered along with deep contacts from insular and opercular electrodes, demonstrating true locations within the amygdala, hippocampus, as well as more laterally in the superior temporal gyrus and short insular gyrus. Additionally, a second smaller cluster of clinically noted contacts in the insula was revealed as well as a set targeting the cingulate within white matter tracts in close spatial proximity to the middle frontal gyrus. *Only left-sided electrodes are included in these montages for simplicity. All color coding follows the legend in panel f.

FIGURE 5  Demonstration of the anatomical framework for an SEEG exploration with atypical anatomy and a Perisylvian seizure network (subject 3). (a) An electrode (L-INSU) with a posterior trajectory targeting the left insula contained several deep contacts truly within the insula and sampling a region of cortical microgyria. (b) On this semi-coronal slice viewing an electrode targeting the parietal cortex, the relabeled electrode emphasizes its placement along the left precentral gyrus. (c) Similarly, a third electrode contained contacts sampling the postcentral gyrus. Notably, clinical seizures from this subject were brief and electrographically subtle, with ictal onset of a large direct current shift followed by low voltage fast activity in L-PAR and L-INSU. (d) A 3D reconstruction of contacts was broadly color-coded by lobe instead of electrode, again following the legend in panel f. Note the cluster of bright red contacts in the frontoparietal region, comprising sections of three separate electrodes, that illustrate how this specific exploration sampled the seizure network. On the traditional montage (e), frontal and parietal lobe contacts were intertwined in the traditional montage, whereas the on the anatomical montage (f), these contacts are clustered together. As a result, at least two seizure nodes emerged on either side of the central sulcus, following the Perisylvian polymicrogyria. As with subject 2, only left-sided electrodes are shown for simplicity and because only left-sided electrodes were noted to be involved in the seizure network.
and seizures is more easily seen across the involved contacts. Our method extends this concept by placing SEEG electrodes, which may encompass a diverse range of trajectories, into a similar anatomic framework to better identify the epileptogenic zone. Indeed, each of the presented examples used to demonstrate its applicability was uniquely complex, as is to be expected for most SEEG explorations. Their typical seizures varied greatly in features including origin, duration, spread, correlation with imaging, and extent to which the seizure onset was captured by lead placement. Given these vast differences that can exist between SEEG investigations, this flexible anatomic approach would greatly standardize the interpretation and communication of data between surgical epilepsy teams.

To date, a practical integrated tool for SEEG contact localization has not yet been accepted clinically. The first report of efficient depth electrode localization using similar software cited access to specialized personnel as an obstacle toward widespread usage (Medina Villalon et al., 2018; Narizzano et al., 2017; Princich et al., 2013). As an illustration of this issue, the 3DSlicer software we used is a popular application for research. Custom SEEG packages have been written for it, but still demand familiarity with the environment and require constant maintenance in order to update dependencies. Our institution overcame this problem by uploading clinically useful outputs to the EMR PACS for our patients, which has not yet been reported or accepted as a common step in the clinical course. This final step crucially and durably brings all useful data to the interpreting epileptologists and other end-users within a pre-existing imaging platform.

FIGURE 6  Comparison of neurophysiological correlation distributions between the traditional and anatomical montages across three subjects. In general, signals within each electrode were only weakly correlated with the group-averaged signal ($r < 0.3$) while anatomically clustered signals were moderately correlated based on Pearson product–moment correlation ($r > 0.3$). (a) Subject 1 had nine total leads over a unilateral exploration, with the anatomical montage demonstrating a significantly greater average signal similarity within regions versus electrodes. (b) The anatomical montage also offered significantly greater signal correlations within regions for subject 2, who underwent a relatively complex 22-lead exploration of the frontal and temporal lobes in both hemispheres. (c) Subject 3 also had 22 leads in a bilateral exploration, with signals organized by the anatomical montage again demonstrating statistically greater correlation to the group signal. (d) When data were aggregated across all three subjects encompassing 53 total leads, the average signal correlations from anatomically grouped contacts were significantly greater compared to electrode-based groupings. Distributions were fitted to a normal or skew normal distribution for visualization, with mean values denoted by dotted vertical lines.
et al., 2018). Clearly the original nomenclature and reading framework should not be completely abandoned and holds valuable information with regards to signal processing and hardware troubleshooting. Institutions, including our own, may understandably maintain the presentation of clinical electrophysiological information. However, re-referencing electrode clusters based on our proposed scheme can provide additional supplementary information in epileptogenic zone localization. For example, an average montage is still reasonable if electrode-based groupings are replaced with anatomical regions of interest and may be advantageous from a source localization perspective. This possible functionality must also be integrated into popular clinical neurophysiology systems. Further work investigating anatomy-based referencing is necessary to determine if it provides clinically significant novel information or improved signal quality.

4.1 | Limitations

Most methods that automatically segment electrodes rely on cortical maps that either register a standard atlas to the patient MRI or use surface-based parcellation to generate regions. We use the latter approach, though both generally assume normal patient anatomy and can therefore lose fidelity in cases of atypical imaging findings. This issue must be taken heavily into consideration given that patients suffering from epilepsy have a higher rate of these abnormalities, either congenital or acquired, and that such features may be part of the epileptogenic region (Abdel Razek et al., 2009). Of the presented cases, the MRI from Subject 3 demonstrated Perisylvian polymicrogyria that adversely affected the cortical segmentation in the region of the left central sulcus and insula. Since even state-of-the-art image processing software cannot anticipate every edge case, manual segmentation may often be necessary for specific subregions and was performed in the area of this cortical malformation.

5 | CONCLUSION

We offer a novel, generalizable labeling strategy for SEEG that is hierarchical and based on patient-specific anatomy. The spatial and neurophysiologic similarity of signals was greater when presented on our anatomical montage. By including our methods into the existing clinical course, neurophysiologists may adopt a more intuitive perspective for characterizing seizure networks.

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CONFLICT OF INTEREST

The authors have declared no conflicts of interest for this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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