Multimodality medical image database for temporal lobe epilepsy

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ABSTRACT

This paper presents the development of a human brain multi-modality database for surgical candidacy determination in temporal lobe epilepsy. The focus of the paper is on content-based image management, navigation and retrieval. Several medical image-processing methods including our newly developed segmentation method are utilized for information extraction/correlation and indexing. The input data includes T1-, T2-Weighted and FLAIR MRI and ictal/interictal SPECT modalities with associated clinical data and EEG data analysis. The database can answer queries regarding issues such as the correlation between the attribute X of the entity Y and the outcome of a temporal lobe epilepsy surgery. The entity Y can be a brain anatomical structure such as the hippocampus. The attribute X can be either a functionality feature of the anatomical structure Y, calculated with SPECT modalities, such as signal average, or a volumetric/morphological feature of the entity Y such as volume or average curvature. The outcome of the surgery can be any surgery assessment such as non-verbal Wechsler memory quotient. A determination is made regarding surgical candidacy by analysis of both textual and image data. The current database system suggests a surgical determination for the cases with relatively small hippocampus and high signal intensity average on FLAIR images within the hippocampus. This indication matches the neurosurgeons' expectations/observations. Moreover, as the database gets more populated with patient profiles and individual surgical outcomes, using data mining methods one may discover partially invisible correlations between the contents of different modalities of data and the outcome of the surgery.

Keywords: Content-based image retrieval (CBIR), medical image processing, segmentation, image databases systems

1. INTRODUCTION

Ever-increasing developments in medical imaging Technology has resulted in huge increase of medical data both in variety and volume. This demands the integration of medical image data with other modalities of patients' information in a multi-modality database system. Most of the database systems designed for this purpose, support only the text-based query language, resulting in either the lack of content-based navigation and retrieval or inefficiency due to the costly procedure of manual annotation. The current content-based approaches show deficiencies when applied to medical image data. In this paper we present a human brain image database system (HBIDS) with its associated image processing and query tools for content-based medical image management, navigation, and retrieval. The focus of this work is on temporal lobe epilepsy. The data include MRI (T1, T2, FLAIR) and SPECT (ictal and interictal) along with the patient's demographic clinical information. We briefly introduce our recently developed segmentation method for brain image information extraction and annotation. The segmentation module makes it possible to map low-level image features to high-level semantic concepts. We can then query the unstructured image data by their contents. The proposed HBIDS examines surgical candidacy among temporal lobe epilepsy surgery.

Quantitative assessment by imaging modalities of a human condition is typically encumbered by large pool of data. The human central nervous system lends itself to detailed study of its structural and functional aspects by several modalities.

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The outcome of such study is crucial in determining operability in situations such as epilepsy. Two primary issues that underline difficulties in current approaches to such analysis are motivating us in this work: (1) Image data cannot be fully described textually. For instance, there is no means by which one can systematically and uniquely describe a textural pattern by a set of characters/numbers, that is, the visual information is unstructured. A text-based query language (e.g., SQL) for retrieval purposes is therefore insufficient. (2) Most of the content-based image retrieval (CBIR) methods take the overall appearance or the global features of the images into account¹⁻⁵. In a few proposed CBIR methods using the local features⁶⁻⁸, the focusing areas (the segmented regions, detected edges, etc.), are not associated with high-level objects, that means they are semantically poor. Therefore, feature extractors and retrieval methods addressed in current CBIR literature cannot be used to distinguish brain images with subtle anatomical differences.

One can classify the CBIR methods based on the features they use into three categories: (1) color-based methods, (2) shape-based methods, (3) texture-based methods. The first category includes the most widely used approaches in CBIR applications⁹⁻¹³. Color-based methods are relatively robust to background complication and independent of image size and orientation¹⁴. The shape-based methods mostly use a feature space, based on the results of applying edge detectors or region growing operators. Due to the 3D-to-2D mapping procedure of photographic imaging, occlusion, shadow and lighting conditions, in general, there is no direct path to recognize the imaged objects from the edges/regions extracted on the image. In our particular medical application, considering the volumetric characteristic of MR imaging we do not have the mentioned problems; however, since brain structures often have multiple edges or missing boundaries, the situation can be even worse. Therefore, in either case, this category of methods does not lead to any aggregation/generalization that semantically correlates the extracted edges or regions¹⁵⁻¹⁷. Texture analysis methods are usually very time consuming. As a result, this category is often ineffective. Note that the texture-based approaches are usually applied to the whole image. In human brain MRI, there are very few cases in which the global texture features can significantly distinguish among semantically desired and undesired image sets. It is worth mentioning one other category of methods, indirectly related to the above categories, which does not quite fit to any of them. This category can be characterized by a paradigm in which the image compression and indexing are considered as dual problems. One of the advantages of this method is that it reduces image storage requirements. In the medical field however, experts usually prefer to see the original images rather than the processed/compressed versions of them. Therefore, the mentioned advantage cannot be gained in our application. Cai, et al.¹⁴ proposed a prototype design for a content-based functional image retrieval database system (FICBDS) for dynamic PET images. This method is based on a three-step functional image data compression technique, which can achieve very high compression ratios without degradation of image quality. Pixel kinetics is encoded during image data compression to achieve image indexing and compression simultaneously; therefore, the proposed method not only supports content-based retrieval, based on kinetic features of the stored functional images, but also reduces image storage size. This method cannot distinguish the active zones with the same signal characteristics originating from two different anatomically adjacent structures. In other words, this method lacks the capability of labeling the functionality with the corresponding/underlying anatomy and vice versa. In our method the anatomical image data are segmented and co-registered with the functional image data, enabling this capability. This feature leads us to a semantically more meaningful retrieval. A complete overview of the recently developed CBIR systems can be also found in Cai's paper¹⁴.

The contents of an anatomical brain image dataset, such as conventional MRI, consist of structures like the hippocampus, parahippocampal gyrus, ventricles, Sylvian fissure, etc. These structures vary widely from one patient to another in their architectures and intensity properties. Two image sets for one individual before and after a cerebral injury or surgical alteration are more similar than those of two patients with the same disease or surgery or those of two normal cases. It is explained by the fact that in most cases a brain disease affects only a small portion of the whole data set, especially in epilepsy cases where the brain may look for the most part anatomically normal. It means that a particular group of patients cannot be tracked within the database just based on global visual characteristics. Considering again the case of two datasets from one individual before and after a brain injury or surgery, one may suggest that transformed versions of the datasets in a particular feature space resolve the problem. In this case, although the two datasets match geometrically pretty well, there is a completely separate part in the feature space showing their difference. However, if this discriminative portion has a low population, it may be easily considered as noise. Also, noise may generate new clusters or wrong classifications. Having the above observation in mind and considering a few recently published papers^{7,18}, we may classify the CBIR methods into two categories: (1) methods that use global features, and (2) methods that use local features. The first category is more popular and widely used, but not suitable (as

we discussed before) in our application. There are a few works in the second category, two of which are mentioned below.

Chu, et al.⁷, proposed a method to retrieve medical images by feature (e.g., shape, size, texture) and content (e.g., spatial relationship among objects) with a spatial and temporal construct. In this method, after segmentation of selected objects of interest and feature extraction, a classification is performed in which a hierarchical structure called Type Abstraction Hierarchy (TAH) represents the knowledge acquired from the feature space. The TAH provides an approximate classification and it can be either constructed automatically, using a clustering method, or manually. A knowledge-based semantic model is proposed to provide a mechanism for accessing and processing spatial, evolutionary, and temporal queries. A query language has been developed as an extension to ODMG's (Object Data Management Group) OQL (Object Query Language) along with a visual query language. The proposed method requires a manual segmentation for the objects of interest and its contribution is mainly in the classification of the extracted image features. Shyu et al.¹⁸ presented a physician-in-the-loop content-based retrieval system for high-resolution computer tomography (HRCT). The pathology bearing regions and a set of anatomical landmarks are delineated when the images are entered into the database. An overall multidimensional index is assigned to each image based on low-level image attributes extracted from the segmented areas. These two methods require experts to manually segment the objects of interest in the image space. This is time consuming and not cost effective.

In this paper, we describe how to develop a human brain image database system (HBIDS) for epilepsy. To remedy the mentioned limitations of the current CBIR methods, we have included a newly developed, automatic, semantically strong knowledge-based segmentation module¹⁹⁻²¹ in the proposed HBIDS. The brain segmentation poses a challenge as brain structures typically have multiple edges or missing boundaries in some parts. Confining our content-based visual extractor routines upon the segmented structures, we map the low-level image features to the semantics associated with the high-level objects defined within the data model. We can then query the unstructured image data by their contents. The proposed HBIDS examines surgical candidacy among temporal lobe epilepsy patients based on their brain images and other data. Moreover, it can discover relatively weak correlations between symptoms, medical history, treatment planning, brain image data, and outcome of epilepsy surgery. The patient data include modalities such as MRI (T1, T2, FLAIR) and SPECT (ictal, interictal) along with patient's demographic and medical information.

This paper is organized as follows. Section II describes the brain segmentation method proposed to localize the CBIR algorithms within the image space. Section III gives a systematic overview of the proposed method describing each individual module of the HBIDS and their inter-relationships. Section IV addresses the HBIDS database conceptual schema with an emphasis on image- and EEG-related tables/entities. Finally, Section V presents the preliminary results and conclusions.

2. BRAIN SEGMENTATION

The novelty of the proposed method is partly due to the integration of a recently developed segmentation method into the HBIDS. Since the hippocampus is an extremely important brain structure, e.g., for epilepsy diagnosis and treatment, the proposed segmentation method is mainly focused on (but not limited to) this structure. The hippocampus is a relatively small structure of the human limbic system. Visual and architectural features of this structure have been studied for epilepsy and Alzheimer's disease²²⁻²⁵. The hippocampus is characterized by multiple edges and missing boundaries. As a result, segmentation of this structure is extremely challenging. We are planning to segment other brain structures of interest for epilepsy (e.g., parahippocampal gyrus). The proposed segmentation method has two steps and is fully automatic. The first step is brain structure localization and the second step utilizes a 3D deformable model to achieve an accurate and high-resolution segmentation.

2.1 Brain structure localization

The localization procedure finds several landmarks around the desired structure. We create binary images representing gray matter (GM) and cerebrospinal fluid (CSF). Using the binary images, the proposed method finds certain landmarks from specified points of view and within specified fields of search. Morphological routines are utilized to extract the connected components/segments of the landmarks. A rule-based system with a set of 35 rules is used to analyze the extracted landmarks and segments. This knowledge-based system assigns each individual landmark an intermediate

confidence factor (ICNF). The ICNF shows how accurately each individual landmark/segment is found. An approximate reasoning procedure calculates an overall confidence factor (CNF) from the ICNFs. Setting a threshold for the CNF, we determine whether the hippocampus exists in a particular slice and how accurately its landmarks are found (See the cited references¹⁹⁻²⁰ for further details). Figs. 1(b)-(c) show the results of hippocampal localization on the coronal and sagittal views of a set of T1-weighted MRI scans.



Figure 1: a) A coronal view of the human hippocampus on a T1-weighted MRI. b, c) Hippocampal localization results on coronal and sagittal views, using the knowledge-based localization method. d, e) The segmentation results on coronal and sagittal views using the 3D deformable model.

2.2 3D deformable model

The proposed 3D deformable model converts the localization results (as an initial polygon) to an accurate and highresolution 3D model of the structure. The task is done by adding more vertices to the initial model and moving them iteratively based on the internal and external forces until the termination condition is met. The internal forces are calculated from local model curvature, using a least-squares error approximation method. The external forces are calculated by applying a step expansion and restoration filter (SEF) to the image data. A solution for self-cutting problem has been proposed via principal axis analysis and re-slicing (See the cited reference²¹ for details). Two orthogonal views (coronal and sagittal) of the final result are illustrated in Figs. 1(d)-(e).

3. HBIDS ARCHITECTURE

The HBIDS is a 3-tier web-based database system, with Oracle database as tier 1 (database server), Apache server as tier 2 (web server) and Tomcat as tier 3 (application server). The disadvantages of web-based design in our application are: (1) data transfer is limited to the network speed; this fact is more sever in our application since medical image dataset is usually very large, (2) since the patients' information is highly confidential, the security issues are more sever. Using login names and passwords, we have protected our system from general unauthorized users. Moreover, users can be categorized into at least three categories with different levels of privileges based on their login names and passwords. The highest authority is granted for the users with insertion, deletion, update and query permissions. This level of authority is for the trained experts within the medical center that owns the HBIDS. The second level does not have

insertion, deletion and update permission, rather, it supports only database query. This level of authority is for physicians and students within the medical center who already have access to patients' information through a conventional database. The third category has query permission in such a way that no patient identification is disclosed. More precisely this category would not have access to the patient's name, SSN and MRN.



Figure 2: HBIDS modular architecture.

Due to the highly confidential nature of patient information, most medical centers do not allow any kind of access to patient information including telnet and ftp from outside of their secure domains. Usually medical centers such as HFHS (Henry Ford Health System) protect their information by firewall software. Keeping the patient information outside a protected/secure domain allows hackers and data thieves access to such sensitive data. Moving the database and web servers inside such secure domain prevents the clients outside the domain to access the database. To solve the problem we are planning to keep the web server outside the secure domain and grant a secure connection to the database server, which is inside the secure domain. We are currently working on the information security with the HFHS IT administrative authorities to resolve the issue. The rest of this section is more about the conceptual architecture of the HBIDS, rather the implementation architecture partly discussed in the previous paragraphs. Fig. 2 shows the main modules of the HBIDS architecture and their interconnections.

There are two categories of data stored in the proposed database: image modalities and non-visual modalities. Nonvisual data modalities include both structured (e.g., demographic info, medical history) and unstructured data (e.g., EEG phase one). Image modalities include MRI (T1, T2, FLAIR) and SPECT (ictal and interictal), which are both unstructured. The medical image processing modules are incorporated into the HBIDS to extract query-relevant information from image data. The knowledge-based segmentation module receives the image data as input and generates the required segmented models. The result of segmentation is stored in the database. The parameters of segmentation module need to be retrieved from database. Therefore, there is a double-arrow shown in Fig. 2 between database and segmentation modules. The registration module gets two modalities of image data and estimates the best transformation matrix that maps one modality on the other. The transformation matrix is stored in the database for each modality of image data. The segmentation models and registration information are retrieved from the database to keep a visual feature extractor confined within the boundaries of an object of interest (e.g., hippocampus) in image space. The features extracted from the image data are sent to clustering/classification module or they are directly stored in the database. The clustering module performs the indexing and the classification module makes the decision if a patient is among the candidates of an issued query. The query module decides which part of information for candidate patients should be retrieved and perhaps how the information should be processed (e.g., averaged) and visualized. The structured portion of the non-visual data is directly stored in the database. The unstructured part needs to be processed according to our proposed data model. The results are stored in the database as structured data.

3.1 Segmentation module

The segmentation module generates a 3D model for the desired brain structures from the specified image modality based on the methods proposed in Section II. This module includes: 1) "Localization parameters estimator" which is a histogram analysis program to determine the threshold values for generating binary images, 2) intrinsic parameters of the 3D deformable model which is a set of fixed parameters for each particular brain structure determined once per structure, 3) "Knowledge-based localization" and, 4) "3D deformable model" as explained in *A* and *B* in Section II, respectively. Fig. 3 highlights the segmentation module and shows its interactions with the other modules of the HBIDS. The input to the segmentation module is a fixed modality of images (T1-weighted MRI in our case) and the intrinsic parameters of the 3D deformable model. The output is the 3D segmented model of the object of interest along with the estimated localization parameters. The intrinsic parameters of the 3D deformable model shows the flow of this information (Fig. 3). Physically, the segmented model is stored in the database along with localization parameters used to build the model. The segmented model is stored as a text file using the VTK (Visualization Tool Kit) format, so that VTK software can be employed to visualize the model as a graphical object. Further, it can be used to augment the 2D brain images with an appropriate graphical 3D view of the model.

3.2 Registration module

The registration procedure makes it possible to label the activated regions in the functional imaging modalities (e.g., SPECT) with the underlying anatomical structures. The dual issue, which is also provided by registration, involves measuring the activity levels of each desired structure. In our application, the segmented model is determined using T1-weighted MRI in which the anatomy is shown very well. In order to use the segmented model for the other modalities, we need an application to align other image modalities with the T1 modality. Doing so, pixels with the same coordinates from two modalities point to the same positions in the image space. As the result we can use the segmented model on the transferred modality. The "Registration Module" does the above job (See the cited reference²⁶ for more details). Fig. 4 highlights the registration module and shows its interaction with the other modules of the HBIDS.



Figure 3: The HBIDS modular architecture: the segmentation module is highlighted.



Figure 4: The HBIDS modular architecture: The registration module is highlighted.

The CRD files, mentioned in Fig. 4, contain 2D contours that outline the patient's head on the corresponding image files. The whole set of CRD files belonging to an image modality determines a 3D surface, which represents the patient's head skin. There are two sets of CRD files extracted from: (1) T1 modality, as the reference dataset, and (2) registered image modality, which is going to be aligned with the T1. An optimization procedure is performed to find the best match of two skin models. The transformation obtained from the optimization procedure is used to transfer the second image modality to the first one (T1). As an optional last step, if we would like to display the corresponding registered slices of the two modalities (image fusion), a re-slicing procedure can be applied. The skin model(s) and transformation matrix are stored in the database. This flow of information is shown in Fig. 4 by an arrow from the registration module to the multi-modality database.

3.3 Visual feature extraction and clustering-classification modules

The visual feature extraction module includes a set of applications each of which calculates a visual feature (e.g., color, texture, shape, and spatial relationship) within the segmented model and in a proper image modality. There are a variety of features such as volume, surface area, intensity mean-value and standard deviation, length, width, and principal vectors that are often of interest. These features are calculated once the segmented model is built. The information is stored along with the segmented model in the database (off-line procedure). Furthermore, there are features we may find of interest later, or do not yet have their application codes. In such cases, we can simply add the new feature extractor when it is available as a new application to the visual feature extraction set. Using the extracted features, the classification module decides if the image set is going to be retrieved (on-line procedure). The result of classification is sent to the query module for further analysis and display to user. The clustering module performs the procedure of unsupervised indexing based on a portion of the extracted features. Fig. 5 highlights the visual feature extraction and clustering/classification modules along with their interactions with the other parts of the HBIDS.

3.4 Query module

The query module acts like a mediator in the sense that depending on the input query, it decides about the job scheduling and flow of information. It decides from which image modality the required information should be retrieved. The query module retrieves the appropriate set of parameters for the 3D deformable model. The decision about which visual feature

extractor should be used is up to the query module. In case the segmentation is already done, the query module may retrieve the model from the database along with an appropriate image modality and its registration transformation matrix for further analysis. Based on the input query, this module decides which parts of the associated data for a candidate patient or group of them should be displayed. Finally, query module analyzes (e.g., averages) the retrieved data and performs the information visualization through a graphical user interface (GUI).



Figure 5: The HBIDS modular architecture: The visual feature extractor module is highlighted.

3.5 Non-visual feature extractors and general information about the HBIDS

For the EEG study, the non-visual feature extractor can be either an 1D signal processing algorithm or an expert/specialist. The experts do this as part of their routine clinical work, based on well-defined standards. For unstructured text information there are two separate routines for old and new patients. For old cases, the information has been stored in the patients' files. In this case the information extractor can be either an expert/trained nurse (data analyst) or natural language analyzer software. We have an expert extract the information. For new cases, the information is stored in the database upon patient presentation and according to a predefined data model. It is therefore treated as structured data. The structured data do not need to be analyzed, so they are directly stored in the database. The system author is either an individual clinician or consortium. The end user could be a clinician or epidemiologist.

4. HBIDS DATABASE SCHEMA

The database includes 47 tables categorized in 6 major groups: (1) patient's personal information, (2) medical history, (3) disease description, (4) image data, (5) EEG analysis, and (6) surgery-outcomes. Although the image data is not the only unstructured data managed in this database, it is the most challenging one. The medical history and disease description for old cases and EEG are also instances of unstructured data in the proposed database. For the latter types of unstructured data, a manual annotation/labeling procedure based on a predefined data modeling is employed as explained in the previous Section. The left most portion of Fig. 6 shows part of the conceptual schema diagram for the EEG-related entities/tables. All seizures during the inpatient video-EEG recording period are analyzed for their time of onset, electrode distribution at onset and duration (in EEG_SZ table). For a regional seizure, many electrode locations are stored in ELECTROD_LOC table. Interictal data (i.e., spikes, sharp and slow waves) are recorded along with the electrode location as attributes of the EEG_PH1 table. Fig. 6 also shows part of the conceptual schema for the image-related entities/tables. IMG_DATA allows for several image modalities to be scanned with no more than one set of

images per day for each modality. The common attributes of the image data set (thickness, resolution, etc) are kept in the IMG_DATA table. Since the focus of our research is on epilepsy, we consider two primary types of modalities for IMG_DATA as subtypes: (1) MRI (T1, T2, and FLAIR), (2) SPECT (ictal and interictal). This structure would allow adding new image modalities in future if needed.

5. PRELIMINARY RESULTS AND CONCLUSIONS

The front-end of the HBIDS is designed to be as user-friendly as possible. We have currently developed 36 forms to allow for storing and browsing/querying the patient data. Each form has an overview menu of the whole data model to the left side, which allows for browsing the patient information. Fig. 7 shows the patient's personal information form that can be used for insertion, deletion, and updating. The left side menu provides the users with an arbitrary access to any view of the data. In some data insertion cases involving a referential constraint, the interface guides the user to a former table that must be populated first.



Figure 6: The conceptual sub-schema diagram for inpatient EEG study (left portion of the dashed line), and image studies (only the key attributes and relationships are shown).

The proposed system renders efficient analysis of brain image data (i.e., MRI, SPECT) along with other data modalities for individual and comparative group studies. Although the HBIDS is focused on epilepsy, the proposed method can be adopted for similar medical applications. As a benefit of adding segmentation to the database, the semantic contents of the image data can be queried. The HBIDS can eventually answer queries such as: "What is the correlation between the attribute_X of the entity_Y and outcome_Z?" where entity_Y can be a brain structure (e.g., hippocampus) and attribute_X can be any attribute of entity_X (e.g., average intensity, volume) and outcome_Z can be any result of an epilepsy surgery (e.g., memory quotient, postoperative seizure class). Queries like the above are crucial for surgery candidacy determination for epileptic patients.



Figure 7: The personal-information form that can be used to insert, delete, and updating the patient's data. The left side shows an overview of the major views of HBIDS and provides users with an arbitrary access.

We have segmented the hippocampus for 24 patients on T1-weighted MRI scans. The attributes of the hippocampus such as volume, surface area, intensity mean-value and standard deviation are calculated based on the segmented model. A query such as "What is the average preoperative volume difference between the right and left hippocampus in patients with left medial temporal lobe epilepsy?" resulted in 275.7 mm³. The database suggests high intensity average within the surgery-candidate hippocampi in FLAIR modality. Fig. 8(d) shows a 3D model of the hippocampus in FLAIR image space. A coronal FLAIR slice is also shown to demonstrate how accurate the model is transferred to the FLAIR image space. Fig. 8(c) represents the corresponding T1 slice overlaid by the original hippocampus model. Note that since the hippocampus model is estimated using T1-weighted images, we have to transfer the model to the FLAIR image space to be able to use it. The transformation matrix calculated by registration module is retrieved from the database for this purpose. Fig. 8(a) and 8(b) show the original hippocampus models in T1 image space, where the latter shows it overlaid on a T1 coronal slice.

Considering again the proposed image databases with manual segmentation, there is one issue we would like to address from a database point of view. The manual segmentation approach is not reproducible. This in part implies that the

manual segmented models are not built based on the same sets of initial conditions and constraints. Therefore, in its nature, manual segmentation violates the principle of integrity constraint. Although this is a conceptual violation, which cannot be detected by a DBMS, but it makes the data incomparable and thus un-retrievable. This is another reason why we have emphasized on an automatic segmentation.

A mapping function from the surgery outcome to the set of real numbers facilitates a more objective surgery assessment. The final goal of this work, which is a surgical candidacy determination, is made possible by a multi-variant approximate reasoning based on the above objective surgery assessment and the conditions of the candidate patient. When the database gets more populated, an optimal mapping function and reasoning framework for decision-making may be established. In this model, the patient is defined as an input point described by a sub-set of the proposed data model including disease description, medical history, radiology and image studies, EEG study, etc. A weighting vector may enforce the *a priori* knowledge or the posterior priorities we may mine from the previous cases regarding the importance of each field of the input data.



Figure 2: a) A 3D visualization of a hippocampus model. b) A T1-weighted MRI slice overlaid with the hippocampus model. c, d) T1 and FLAIR MRI of a coronal slice where FLAIR images are registered on T1 and both are overlaid with the hippocampus model.

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