A CAD System for Hemorrhagic Stroke

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SUMMARY – *Computer-aided detection/diagnosis (CAD) is a key component of routine clinical practice, increasingly used for detection, interpretation, quantification and decision support. Despite a critical need, there is no clinically accepted CAD system for stroke yet. Here we introduce a CAD system for hemorrhagic stroke. This CAD system segments, quantifies, and displays hematoma in 2D/3D, and supports evacuation of hemorrhage by thrombolytic treatment monitoring progression and quantifying clot removal. It supports seven-step workflow: select patient, add a new study, process patient's scans, show segmentation results, plot hematoma volumes, show 3D synchronized time series hematomas, and generate report. The system architecture contains four components: library, tools, application with user interface, and hematoma segmentation algorithm. The tools include a contour editor, 3D surface modeler, 3D volume measure, histogramming, hematoma volume plot, and 3D synchronized time-series hematoma display. The CAD system has been designed and implemented in C++. It has also been employed in the CLEAR and MISTIE phase-III, multicenter clinical trials. This stroke CAD system is potentially useful in research and clinical applications, particularly for clinical trials.*

Introduction

Stroke, or brain attack, is a sudden onset of neurological injury vascular in origin disturbing cerebral perfusion. It is a leading cause of death in the world and the major cause of permanent disability. Stroke has a great impact on public health and a high cost for primary treatment, rehabilitation, and chronic care. There are two types of stroke: ischemic and hemorrhagic. Ischemia is an effect of parenchymal hypoperfusion due to interruption of blood flow to the brain existing sufficiently long enough. Hemorrhage develops as a result of bleeding directly into the brain.

Each type of stroke requires different treatment. Thrombolysis is the main treatment for acute ischemic stroke by administering recombinant tissue plasminogen activator (rt-PA) intravenously and/or intra-arterially through a microcatheter. There are several ways to treat hemorrhagic stroke. One of them is to evacuate the hemorrhage surgically by performing craniotomy. This preferred approach additionally facilitates decompression. A recent study

of early surgery versus initial conservative treatment in patients with spontaneous supratentorial lobar intracerebral hematomas confirms that early surgery might have a small advantage¹. A less invasive approach is to insert a catheter into the ventricular system and lyse the blood clot by administering rt-PA. The hemorrhagic stroke computer-aided detection/diagnosis (CAD) system addressed here supports the latter procedure.

Intraventricular hemorrhage (IVH) is bleeding into the ventricular system and it often results from severe intracerebral hemorrhage (ICH). Two randomized, phase-III clinical trials: CLEAR III (Clot Lysis Evaluating Accelerated Resolution of Intraventricular Hemorrhage) and MISTIE III (Minimally Invasive Surgery plus rt-PA for Intracerebral Hemorrhage Evacuation) tested the use of rt-PA for hemorrhagic stroke treatment². The procedure requires a catheter to be inserted into the ventricular system, rt-PA administered through it, and a series of non-contrast computed tomography (NCCT) scans acquired to monitor the outcome of clot lysis. For each scan, a he-

matoma (IVH jointly with ICH) must be evaluated (segmented), its volume measured, and treatment progression assessed in terms of hematoma volume reduction. NCCT is a technique for hemorrhage evaluation as it is fast, sensitive to blood, and available in most hospitals and emergency departments. Hematomas on NCCT vary in shape, size, location, density (intensity), contrast and texture. Segmentation of hematomas depends on many factors, such as partial volume effect (volume averaging), fuzzy and low contrast borders, noise, beam hardening, motion artifacts, head tilt, and incomplete head coverage.

CAD has become a part of routine clinical practice, increasingly used for quantification and decision support as well as for detection and interpretation of diseases of various organs^{3,4} and the whole body⁵. CAD is well established clinically in mammography⁶⁻⁹, colonoscopy^{10,11} and chest imaging^{12,13}. Despite a critical need, there is no clinically accepted CAD system for stroke yet.

We are in the process of developing a suite of stroke CAD systems for acute ischemic stroke¹⁴⁻¹⁶ (including one handling NCCT only¹⁷), hemorrhagic stroke, stroke outcome prediction¹⁸ and stroke in the emergency department (ED)¹⁹. These CAD systems provide functions for image viewing, image processing, 3D display and manipulation, quantification, atlas to scan mapping, and atlas-assisted analysis. The aim of this work is to present the design and development of the CAD system for hemorrhagic stroke. We also describe its features for handling of IVH and ICH, suitable to support the CLEAR and MISTIE multicenter clinical trials.

Methods

The hemorrhagic stroke CAD system monitors progression and quantifies blood clot removal. The clot is automatically segmented on each scan and, if necessary, it can be further edited by means of a dedicated contour editor. The clot is displayed in 2D and 3D, interactively manipulated, and its volume measured. In addition, the system provides tools for progression assessment by analyzing time series, and visualization of the catheter(s) along with the clot. We address the design of the main components of the CAD system: workflow with the corresponding functionality, system architecture, and user interface.

Workflow

This CAD system supports a following seven-step workflow: select patient, add a new study, process patient's scans, show segmentation results, plot hematoma volumes, show 3D synchronized time series hematomas, and generate report.

Select patient. The user first selects the patient's data, and the CAD system reads them in DICOM format and opens this patient for processing.

Add study. A new study is added to the currently open patient; the patients are typically scanned on a daily basis.

Process. For the selected studies, this step automatically segments the hematoma, segments the catheter(s), and measures the volume of the segmented hematoma.

Show hematoma segmentation results. The segmentation results are shown on axial, coronal and sagittal images along with a 3D model (the actual algorithm employed for segmentation is referred to and briefly described below). In this step, the user can employ the contour editor to edit the segmented results (contour files) and interactively subdivide the hematoma into IVH and ICH compartments.

Show volume plots. In order to assess the dynamics of hematoma evolution and the treatment progression measured as a clot volume reduction, volume plots of the complete hematoma (IVH+ICH) and separately IVH and ICH over time are shown. In addition, a reference line with an 80% volume drop is drawn on the hematoma volume plot.

Show 3D synchronized time series hematomas. All the segmented and reconstructed in 3D hematomas along with their IVH and ICH compartments, each generated per single study, are synchronously displayed and their corresponding volumes are given. If needed, the catheter(s) reconstructed in 3D can be included.

Three groups of operations are available for 1) 3D model manipulation and display (rotate, zoom and pan), 2) 3D model smoothing (as scans, typically, have a high slice thickness causing blocky 3D reconstructions), and 3) settings (orientation, time series matrix, and additional information, such as midsagittal plane, brain bounding box, and directions).

Generate report. A report is generated with a patient ID, list of studies, and for each study the volumes of hematoma and its IVH and ICH compartments.

Figure 1 4-component architecture of the hemorrhagic stroke CAD system.

Architecture

The system architecture contains four main components: library (toolkit), tools, application along with the user interface, and hematoma segmentation algorithm (Figure 1).

The toolkit contains the basic building blocks (functions) for image file format reading and writing as well as mathematical, graphical and image processing operations. There are several tools useful for stroke image handling, such as the contour editor, 3D surface modeler, 3D volume measure, histogramming, windowing (interactive and presets), region of interest readout, atlas-to-scan registration, and atlas-assisted (localization) analysis along with brain atlases of anatomy, blood supply territories (BST), and cerebral vasculature (employed at present in the ischemic stroke CAD¹⁵ and stroke CAD in the ED¹⁹).

A powerful yet easy to use contour editor allows the user to edit the segmented clots. The user edits interactively the outline of a clot by creating, moving and deleting contours as well as by moving, adding and removing contour points. This is done very precisely by zooming into the edited region and enhancing the accuracy of clot delineation. A 3D surface model of a clot is reconstructed from its 2D contours by generating a binary volume from the voxels encompassed by these contours and applying the Marching Cubes algorithm²⁰ to this volume. The 3D model can be interactively displayed and manipulated (rotated, zoomed and panned) in 3D. The core of this CAD system is the algo-

rithm for hematoma segmentation. We have developed so far several algorithms for hematoma segmentation and evaluated their performance earlier²¹⁻²³. In this design, the algorithm is decoupled from the application (Figure 1), so we can continuously enhance the segmentation algorithm to increase its performance and robustness to data variations.

User Interface

The user interface contains a main window composed of four views and a control panel supporting the workflow operations. The views comprise the original axial and orthogonally reformatted coronal and sagittal NCCT images, and a 3D model of a hematoma. The user is able to display all four views or any selected one. There are three additional pop-up windows to show acquisition parameters, hematoma volume plot, and 3D synchronized time series hematomas with local controls.

Results

The CAD system has been designed and implemented in C++ according to the architecture presented in Figure 1. It has been employed to date at Johns Hopkins Hospital, Baltimore, MD, USA in the CLEAR and MISTIE phase-III, multicenter clinical trials. The user interface of the CAD system is presented in Figure 2. Figure 3 illustrates a hematoma volume plot and a 3D synchronized time series hematoma

Figure 2 User interface of the hemorrhagic stroke CAD system with four views and the control panel (on the right). The slice thickness of the NCCT scan is 5 mm causing blocky hematoma outlines on the coronal and sagittal images. The 3D model has been smoothed.

display of a patient with nine NCCT studies acquired over ten days.

Discussion

The hemorrhagic stroke CAD system introduced here provides functions to segment, quantify, and display hematoma in 2D and 3D, and additionally supports the evacuation of hemorrhage by thrombolytic treatment through a catheter inserted into the ventricular system. This system aims at progression and quantification of blood clot removal. The clot is automatically segmented from NCCT time series and its volume is measured over time. Recently for clot segmentation, the algorithm²¹ has been employed based on texture energy. An NCCT scan is windowed, skull stripped, convolved with textural energy masks, and segmented using a combination of thresholding and fuzzy c-means. Artifacts are removed by statistical analysis and morphological processing.

The segmented clot can be displayed in 3D along with a catheter (or multiple catheters).

The user is able to interactively fine tune the automatically segmented clot by means of the contour editor to potentially enhance the hematoma delineation. In particular, the 2D-3D correlation quickly identifies any false positives in hematoma segmentation, which may be caused by the dura mater and partial volume effect around the catheter, bone, and calcification.

The hematoma volume plot captures the trend in hematoma volume changes and facilitates decision-making based on the hematoma volume size (Figure 3A). It should be noted that despite a hematoma volume drop visible on the hematoma volume plot, new bleeding may occur. Therefore, a synchronized display of 3D time series hematomas enables the operator to observe and identify any new bleeding by comparing the neighboring hematoma time instances in 3D. Another advantage of synchronized display is a dynamic presentation and monitoring of the process of clot lysis (see Figure 3B).

The core of the design is that the CAD application is detached from the segmentation algorithm, so each of them can be benchmarked and enhanced independently. This is particu-

A

B

Figure 3 Processing of a patient with 9 NCCT studies acquired over 10 days. A) Volume plot. B) 3D synchronized time series hematoma display (note a dynamic process of clot lysis).

larly important for the hematoma segmentation algorithm. It should be noted that segmentation of hematomas is not an easy task. In order to better understand hematoma properties, we have recently studied IVH and ICH on serial NCCT²⁴. Hematoma is characterized by 59.0 HU mean, 60.0 HU median, 11.6 HU standard deviation, 23.9 HU mean contrast and -0.24 skewness. The change in hematoma density with hematoma aging is -0.99 HU/day. The intersection point of the mean gray matter-hematoma density distributions is at 55.6 ± 5.8 HU. As the hematoma distribution substantially overlaps with that of gray matter, manual segmentation of hematoma is difficult and automatic density-based segmentation impossible. Therefore, future automatic algorithms for hematoma segmentation should take into account hematoma staging as well as contrast between hematoma and parenchyma.

As the human brain is the most complex living organ, the development and validation of CAD systems for the brain are much more complicated than these for other organs, such as the chest, colon and breast. Complex decision-making, dynamics of changes, and lack of reference standards (such as the one we have proposed for IVH/ICH in²⁴) are also limiting factors. Most research efforts aim at developing CAD systems for detection of brain tumors by employing various techniques and modalities²⁵⁻²⁹. Other efforts involve detection of intracranial aneurysms³⁰, cerebral microbleeds³¹ and multiple sclerosis lesions³²; diagnosis of movement disorders³³ and Alzheimer's disease³⁴; and providing fusion of brain images³⁵.

Only a few CAD systems support stroke to a limited extent. WebParc provides measures of stroke lesion volume and location with respect to a registered brain template³⁶. A CAD system³⁷ aims at improvement of the accuracy of radiologists' performance in detection of lacunar infarcts on T1- and T2-weighted images. A CAD system³⁸ objectively and interactively characterizes the atherosclerotic plaque by incorporating scores to determine the risk of plaque rupture (and thus of brain stroke) and uses several tools to outline the plaque and compute different echogenicity measures. A CAD system³⁹ aids in detection of small acute intracranial hemorrhages. Another CAD system⁴⁰ is for early detection of ischemic stroke with small lesions using image feature characteristics. To our best knowledge, this work addresses the first CAD system for detection, quantification, and visualization of hemorrhagic stroke.

This stroke CAD does not provide localization achievable by means of brain atlases or templates, as already available for ischemic lesions¹⁵ and provided, for instance, by *WebParc*³⁶. One of the reasons is that anatomical deformations in hemorrhagic stroke are much higher than in ischemic stroke scans; moreover, hemorrhage processing is not so time critical. Therefore, fast atlas-to-scan registration techniques employed in ischemic stroke are not the most effective in hemorrhagic stroke.

Atlas-based analysis, introduced by us to stroke image processing^{15,16}, has several advantages. After atlas-to-scan mapping, multiple atlases are superimposed (in image or contour representation) with a user-controlled blending onto the studied scans or maps and employed to obtain the underlying anatomy and BST. The user can point to any location in the displayed image and obtain the anatomy and BST labels as well as inspect which anatomical structures and BSTs are within the clot or infarct. The approach automatically analyzes the entire regions occupied by the lesion (a clot or infarct) and calculates: 1) names of all anatomical structures and blood supply territories involved in the lesion, 2) volume of occupancy for each structure and territory, and 3) percentage of occupancy for each structure and territory.

Future work not only aims to increase the performance of the CAD system (in terms of functionality, tools and user interface) and improvement of hematoma segmentation (in terms of accuracy, robustness and speed), but also to address some open design questions, such as how to balance automation and interactivity as well as clinical and research needs. For instance, a single "Go" button solution may be preferred by some clinicians whereas others may favor a set of interactive tools allowing them to control, support and enhance each step of the workflow. Another issue is how much results, whose analysis is time-consuming, shall be provided to the clinician. For example, is analysis of a single IVH hematoma sufficient or shall the clinician be provided with the parcellation of an IVH into ventricular compartments to analyze all of them? Finally, validation of this CAD in a clinical setting at multiple sites is needed with a cost-benefit analysis.

In summary, this stroke CAD system provides quantitative assessment and supports decision-making in thrombolytic treatment of hemorrhagic stroke. It is potentially useful

in research and clinical applications, particularly, for clinical trials. The CAD system is employed at present in the CLEAR and MISTIE phase-III clinical trials.

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