OSIRIX™ AS A FEASIBLE TOOL FOR IN OFFICE MANUAL HIPPOCAMPAL VOLUMETRY IN THE ELDERLY: A TECHNICAL NOTE

INTRODUCTION: Manual tracing is an effective method to measure hippocampal volume. OsirX™ is a Digital Imaging and Communications in Medicine (DICOM) viewer with an intuitive user interface that has been widely used by radiologists and other specialists in their daily practice. OBJECTIVE: To describe OsirX™, a tool for in office manual measurement of hippocampal volume. METHODS: The open-source OsirX™ viewer was used with three dimensions (3D) T1 weighted spoiled gradient recalled echo (SPGR) sequence images, with 1 mm slice thickness and 0.1mm gap (voxel size 1 mm³). Magnetic Resonance Imagings (MRI) were obtained on a 1.5 T system. The entire procedure lasted less than 15 minutes for each hippocampus. CONCLUSION: OsirX™ viewer is a feasible tool for in office manual hippocampal measurement. There is no standard hippocampal volume for Alzheimer’s disease, thus comparison could be regarded as the rate of hippocampal atrophy over time, correlated with clinical evaluation and cognitive tests.

KEYWORDS: hippocampus; magnetic resonance imaging; Alzheimer disease.

RESUMO

INTRODUÇÃO: O traçado manual é um método eficaz de medição do volume hipocampal. Osirix® constitui um visualizador Digital Imaging and Communications in Medicine (DICOM®) intuitivo e amplamente difundido por radiologistas e demais especialistas na sua prática diária. OBJETIVO: Descrever protocolo de medição volumétrica manual do hipocampo com o visualizador Osirix®. MÉTODOS: Foi utilizado Osirix®, com imagens de sequência volumétrica spoiled gradient recalled echo (SPGR) ponderadas em T1, com cortes de 1 mm de espessura; intervalo de 0,1 mm (tamanho do voxel 1 mm³). Imagens de Ressonância magnética foram obtidas em um aparelho de 1,5 T. O procedimento durou menos de 15 minutos para cada hipocampo. CONCLUSÃO: O visualizador Osirix® é uma ferramenta prática para volumetria manual do hipocampo no consultório. Não há um padrão estabelecido de volumetria para a doença de Alzheimer, portanto a comparação poderia ser a taxa de atrofia do hipocampo ao longo do seguimento correlacionado com a avaliação clínica e testes cognitivos.

PALAVRAS-CHAVE: hipocampo; imagem por ressonância magnética; doença de Alzheimer.
INTRODUCTION

The hippocampus is one of the brain regions involved in declarative memory. Reduced volume of temporal lobe structures has been used as a biomarker of preclinical and clinical stages of neurodegenerative disorders, with reports of volume reduction in mild cognitive impairment and established Alzheimer’s disease. Despite technological advances in this field, manual tracing remains the most effective method at the lowest cost and is, therefore, still considered the gold standard for validation of automated segmentation algorithms. However, this method is time consuming, limiting its application in clinical and epidemiological practices.

OsiriX™ (Pixmeo, Geneva, Switzerland, http://www.osirix-viewer.com/) is a Digital Imaging and Communications in Medicine (DICOM) viewer that is available in several versions, including the 32-bit version, which is an open-source for Apple computers. OsiriX™ has been designed for image reading and processing. This application has an intuitive, user-friendly interface. Consequently, it has been widely used by radiologists (the Food and Drug Administration approved version) and other image specialists who deal with Digital Imaging and Communications in Medicine (DICOM) in daily practice. It is important to note that neither the U.S. regulatory agency for health-related services (Food and Drug Administration – FDA) nor the Brazilian regulatory agency (Agência Nacional de Vigilância Sanitária – ANVISA) have approved the open-source version for a broader clinical use. In this study OsiriX™ was used to manually measure the hippocampal volume.

The aim of this study was to describe a protocol for OsiriX™ use as a feasible tool for in office manual measurement of hippocampal volume using daily computational resources.

METHODS

Sample

A convenience sample of 12 women (73.6 ± 6.7 years-old) participated in the study. Participants were recruited among outpatients of the Multidisciplinary Center for the Elderly at the University Hospital of Brasilia, Brazil, among those aged ≥ 60 years without a complaint of forgetfulness and who had recently underwent Magnetic Resonance Imaging (MRI) for clinical indication as aches, migraine or other non-mental complaints. Patients were eligible if they were able to provide written informed consent and did not meet clinical criteria for mild cognitive impairment or dementia according to the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV). Patients with contraindications to MRI, or a history or imaging findings of brain disease, such as ischemia, subdural hematoma, hemorrhage, hydrocephalus, tumor, or brain surgery were excluded. The finding of hyperintense white-matter foci on MRI was not considered an exclusion criterion.

All patients underwent a comprehensive clinical assessment detailing clinical history and physical examination. The study was approved by the Research Ethics Committee of Brasilia University School of Medicine (protocol no. 080/2011).

Neuroimaging technique

MR images of the brain were obtained on a 1.5 T clinical MRI system (General Electric Medical Systems, Milwaukee, WI) equipped with an 8-channel head-coil.

The image acquisition protocol included sagittal T1-weighted, axial FLAIR, gradient echo, T1-weighted, T2-weighted, diffusion-weighted, and coronal T2-weighted sequences. We added to this protocol sequences for hippocampal volumetric study (dementia protocol – coronal FLAIR and T2-weighted images perpendicular to the hippocampus) and three-dimensional T1-weighted gradient-echo sequences (spoiled gradient-recalled echo [SPGR] images – repetition time [TR]: 12 ms, echo time [TE]: 5 ms), performed with 1 mm slice thickness and a 0.1 mm gap – voxel size 1 mm³. All MR images were evaluated by a board radiologist for their quality and any relevant findings, as well as for exclusion of patients with any structural damage.

Delineation of the hippocampus

The OsiriX™ 32-bit, version 5.6, was downloaded from the Pixmeo website (http://www.osirix-viewer.com/Downloads.html) on an Apple MacBook Air (1.8 GHz IntelCore i5 processor, IntelHD Graphics 4,000 512 MB, 4 GB of 1,600 MHz DDR3 RAM) using OSX operating system, version 10.8.5. Once downloaded, OsiriX™ performs offline.

Hippocampal volumetric measurements were performed by two readers, both third-year radiology residents (Readers 1 and 2). Visual delineation of hippocampal boundaries was performed according to the guidelines of the Harmonized Protocol for Hippocampal Segmentation (http://www.hippocampal-protocol.net), with variations as described below.

• Anterior border: At this level, it is difficult to identify the hippocampus located below the amygdala. Therefore, we waited for the alveus to appear superiorly or the cerebrospinal fluid of the ventricle to define a lateral-inferior boundary of the hippocampus before starting the measurement.

• Superior border: The hippocampus is located below the white matter boundary of the alveus, fimbria, and cerebrospinal fluid of the lateral ventricle.
• Inferior border: The hippocampus is the gray matter located above the white matter of the parahippocampal gyrus (Figure 1).
• Lateral border: The cerebrospinal fluid of the lateral ventricle defines the lateral boundary of the hippocampus.
• Superior medial border: The cerebrospinal fluid of the ambient cistern defines the superior medial border.
• Inferior medial border: An irregular line separates the white matter of the parahippocampal gyrus (below) from the gray matter of the hippocampus (above).
• Posterior border: We chose a boundary different from that described in the harmonized protocol, that is, visualization of the crus of the fornix at its maximum extent bilaterally, as our last measurement because this structure can be easily visualized at this level\textsuperscript{10} (Figure 2).

Figure 1 Anterior, superior and inferior borders of the hippocampus
Manual hippocampal volumetry

Each hippocampus (right and left) was assessed individually. At least 10 slices were chosen from the anterior border to the posterior end of the hippocampus, preferably when there was a change in its visual conformation. The region of interest (ROI) — the hippocampus in this case — was manually traced (mouse-drawn) on each slice using the brush tool (brush size 1) in drawing mode. The brush tool can be selected by pressing “B” on the keyboard and then choosing between “draw” and “erase”, brush size ranges from 1 to 20 (Figure 3). Then, the whole area was filled in with brush size 2. At this stage, it was possible to correct the path using the brush in erasing mode, if necessary. After manual tracing, we selected “ROI” in the toolbar and we chose “ROI volume” and then “generate missing ROI” to automatically generate the subsequent areas (Figure 4). After that, each new image

Figure 2 Lateral, medial and posterior borders of the hippocampus
was reviewed for manual correction of possible software-related errors. Finally, we repeated the ROI and ROI volume sequence to calculate, using the command “compute volume”, the total volume of all areas of interest and generate a corresponding 3D image. The entire procedure lasted less than 15 minutes for each hippocampus.

**DISCUSSION**

There are several different protocols to measure the hippocampus manually using OsiriX™. A few of them are used in studies that evaluate patients with cognitive impairment and Alzheimer’s disease, while others assess children and adolescents with epilepsy. Unlike the other studies, there was no correction for atrophy related to aging and individual variability. MRI-based semi-automated and automated methods are also currently used to estimate the volume of brain structures. Fully-automated procedures, which operate at an advanced technological level, allow faster measurements in larger samples with minimal or no human input. However, access to this technology is limited, the method is expensive, the algorithms are complex, and the technique requires specialized training. Despite being time consuming, which limits its application in routine clinical and epidemiological practices, manual segmentation in turn provides a reliable demarcation of the boundaries of the structure under investigation.

The protocol described in this study has some advantages. It can be applied to MR images obtained on scanners usually available in public and university hospitals without the need to purchase expensive hardware or software. Furthermore, additional sequences for hippocampal volumetric study are not significantly time consuming in the evaluation and thus can be added to other routinely protocols. OsiriX™ DICOM™ viewer is of easy access and low cost because it is available for free download. In addition, the intuitive interface enables its use in office by referring physicians and other specialists with little DICOM experience.

Our study has some limitations. First, the lower the resolution of MRI, the more difficult the visualization of structures, consequently leading to less accurate tracing of the area of interest, therefore images of poor technical quality should be excluded. Another shortcoming is the fact that some borders are difficult to be properly delineated, thus requiring training. Indeed, the procedure requires effort and time.
To date, there are no widely accepted standards for hippocampal volume in regard to age- or disease-related atrophy levels or on what concerns normal variability among subjects. So, our method may advance research concerning standard volumes for Alzheimer’s disease patients in the Brazilian population, also rendering a basis for comparison by means of a rate of hippocampal change (e.g.: atrophy) over time, rather than considering only one measurement of hippocampal volume at the onset of symptoms.

Thus, geriatricians could take in office manual measurements of hippocampi volume of two or more MRI that would take approximately one hour and correlate the findings with clinical evaluation and cognitive tests.

CONCLUSION

This study evaluated the feasibility of OsiriX™ use for in office manual measurement of hippocampal volume. The entire procedure lasted less than 15 minutes for each hippocampus. OsiriX™ viewer may be considered a feasible tool for in office manual hippocampal measurement.

ACKNOWLEDGEMENT

We are grateful to our colleagues at the Imaging Center and at the Multidisciplinary Care Center for the Elderly of the University Hospital of Brasilia, Brazil.

CONFLICT OF INTERESTS

The authors report no conflict of interests.

Author’s contributions

L.L. Louzada, T.N. Morato, R.E.F. Almeida: contributed to the acquisition and interpretation of the data; drafting the manuscript.

E.F. Camargos, O.T. Nóbrega, L. Farage: contributed to the conception and design of the work; the analysis and interpretation of the data; revising the manuscript.

REFERENCES


