

Alma Mater Studiorum Università di Bologna  
Archivio istituzionale della ricerca

A critical appraisal of Monro's erroneous description of the cerebral interventricular foramina: Age-related magnetic resonance imaging spatial morphometry and a proposed new terminology

This is the final peer-reviewed author's accepted manuscript (postprint) of the following publication:

*Published Version:*

A critical appraisal of Monro's erroneous description of the cerebral interventricular foramina: Age-related magnetic resonance imaging spatial morphometry and a proposed new terminology / Matys T.; Brown F.S.; Zaccagna F.; Kirollos R.W.; Massoud T.F.. - In: CLINICAL ANATOMY. - ISSN 0897-3806. - STAMPA. - 33:3(2020), pp. 446-457. [10.1002/ca.23560]

*Availability:*

This version is available at: <https://hdl.handle.net/11585/871845> since: 2022-02-28

*Published:*

DOI: <http://doi.org/10.1002/ca.23560>

*Terms of use:*

Some rights reserved. The terms and conditions for the reuse of this version of the manuscript are specified in the publishing policy. For all terms of use and more information see the publisher's website.

This item was downloaded from IRIS Università di Bologna (<https://cris.unibo.it/>).  
When citing, please refer to the published version.

(Article begins on next page)

This is the final peer-reviewed accepted manuscript of:

Matys T, Brown FS, Zaccagna F, Kirolos RW, Massoud TF.

*A critical appraisal of Monro's erroneous description of the cerebral interventricular foramina: Age-related magnetic resonance imaging spatial morphometry and a proposed new terminology.*

Clin Anat. 2020 Apr;33(3):446-457

The final published version is available online at: <https://doi.org/10.1002/ca.23560>

#### Rights / License:

The terms and conditions for the reuse of this version of the manuscript are specified in the publishing policy. For all terms of use and more information see the publisher's website.

*This item was downloaded from IRIS Università di Bologna (<https://cris.unibo.it/>)*

***When citing, please refer to the published version.***

ORIGINAL COMMUNICATION

## **A Critical Appraisal of Monro's Erroneous Description of the Cerebral Interventricular Foramina: Age-Related MRI Spatial Morphometry and a Proposed New Terminology**

**Tomasz Matys<sup>1\*</sup>, Fraser S. Brown<sup>1</sup>, Fulvio Zaccagna<sup>1</sup>, Ramez W. Kirolos<sup>2</sup>,  
and Tarik F. Massoud<sup>3\*</sup>**

<sup>1</sup>Section of Neuroradiology, Department of Radiology, Addenbrooke's Hospital, University of Cambridge School of Clinical Medicine, Cambridge, CB2 0QQ, UK.

<sup>2</sup>Department of Neurosurgery, National Neuroscience Institute, Singapore 308433.

<sup>3</sup>Division of Neuroimaging and Neurointervention, and Stanford Initiative for Multimodality neuro-Imaging in Translational Anatomy Research (SIMITAR), Department of Radiology, Stanford University School of Medicine, Stanford, California, USA

**\*Correspondence to:**

Professor Tarik F. Massoud, MD, PhD; Director, SIMITAR; Department of Radiology; Stanford University Medical Center; 300 Pasteur Drive, Grant Bldg. S-031, Stanford, CA 94305-5105, USA. Tel: +1 650-7247026; Fax: +1-650-4985374; Email: [tmassoud@stanford.edu](mailto:tmassoud@stanford.edu)  
or

Dr. Tomasz Matys, MD, PhD; Department of Radiology, Addenbrooke's Hospital, University of Cambridge School of Clinical Medicine, Hills Road, Cambridge, CB2 0QQ, UK. Tel: +44-1223-336894; Fax: +44-1223-330915; Email: [tm418@cam.ac.uk](mailto:tm418@cam.ac.uk)

**Abbreviated title:**

Morphometry of Foramen of Monro

This paper has not been published and it is not under consideration for publication elsewhere

## **A Critical Appraisal of Monro's Erroneous Description of the Cerebral Interventricular Foramina: Age-Related MRI Spatial Morphometry and a Proposed New Terminology**

### **ABSTRACT**

Anatomic connections between the cerebral lateral and third ventricles have been mischaracterized since Monro's original erroneous description of his eponymous foramina (FoMs) as being only one T-shaped passage. Accurate knowledge of the in vivo three-dimensional (3D) configuration of FoM has important clinical neuroendoscopic, neurosurgical, and neuroimaging implications. We retrospectively analyzed volumetric high-resolution brain MRIs of 100 normal individuals to characterize the normal spatial anatomy and morphometry for each FoM. We measured the true anatomical 3D angulations of FoMs relative to standard neuroimaging orthogonal planes, and their minimum width, depth, and distance between the medial borders of bilateral FoMs. The right and left FoMs were separate, distinct, and in a V-shaped configuration. Each FoM was a round, oval, or crescent-shaped canal-like passage with well-defined borders formed by the semicircular concavity of the ipsilateral fornix column. The plane of FoM was angled on average  $56.8^{\circ} \pm 9.1^{\circ}$  superiorly from the axial plane,  $22.5^{\circ} \pm 10.7^{\circ}$  laterally, and  $37.0^{\circ} \pm 6.9^{\circ}$  anteriorly from the midsagittal plane; all these angles changing significantly with increasing age. The mean narrowest diameter of FoM was  $2.8 \pm 1.2$  mm, and its depth was  $2.5 \pm 0.2$  mm. Thus, the true size and orientation of FoM differs from that depicted on standard neuroimaging. Notably, in young subjects FoM has a diameter smaller than its depth, a configuration akin to a short, small canal. We propose that the eponym 'Monro' no longer be associated with this structure, and the term 'foramen' be abandoned. Instead, FoM should be more appropriately re-named as the 'interventricular canaliculus', or IVC, for short.

**Key Words:** lateral ventricle; neuroendoscopes; neuroimaging; third ventricle

## INTRODUCTION

The interventricular foramen (Terminologia Anatomica code A14.1.08.411) is a short conduit between each lateral and the third ventricle of the brain (Tubbs et al., 2014). It is also known by its eponymous name, the foramen of Monro (FoM), after Alexander Monro *secundus* presented its first detailed description in Edinburgh in 1783, and again in 1797 (Monro, 1783; Sharp, 1961; Wu et al., 2012; Tubbs et al., 2014; Patel et al., 2018). FoM is bounded by the fornix, the anterior pole of the thalamus and the choroid plexus. The fornix constitutes the superior and anterior margin, whereas the anterior pole of the thalamus forms the inferior and lateral margins, and the choroid plexus spans the space between the fornix and the anterior thalamus.

Since the time of Monro's description, the number, shape, and size of the connections between the lateral and third ventricles have been confusingly characterized as either one foramen or two foramina, often depending on whether or not the word "each" is used to qualify the foramen, or if the lateral ventricle(s) are referred to in this description in the singular or plural. More specifically, Wilder (1880) described that by his time, seven prior anatomical accounts had considered the FoM as a single foramen, and 13 accounts were of two foramina. Moreover, FoM has been described in general as being either T-shaped (Monro, 1783), Y-shaped (Harisinghani et al., 2011; Glastonbury et al., 2011; anatomyEXPERT, 2019), or V-shaped (Thorek, 1985). Recently, FoM has also been labeled as being "less than one centimeter" in size (Cai et al., 2015), which is a marked exaggeration of the size for a normal FoM in the absence of ventriculomegaly.

Continued lack of appreciation and mischaracterization of the gross anatomy of FoM can indeed be traced back to the well-publicized erroneous original description of the interventricular foramen by Monro himself as a T-shaped passage composed of two interventricular foramina joined through a transverse canal, and a third foramen supposedly leading from the transverse canal into the roof of the third ventricle (Monro, 1783). Regarding that description of FoM, it is theoretically conceivable that the anatomic specimen(s) available to Monro at the time may have been considerably distorted owing to post-mortem or specimen preservation changes (Woollam

and Millen, 1953), or underlying pathology such as hydrocephalus (Raybaud, 2018). We know, for instance, that Monro's first formal description of FoM during a lecture in 1783 concerned his findings from dissections of the brain of a child suffering from hydrocephalus (see below).

Could the full extent of Monro's error in describing his eponymous foramen, and by contrast, its true anatomy and morphometry, be better appreciated in a more realistic *in vivo* context? Indeed, knowledge of the precise three-dimensional (3D) configuration and dimensions of FoM are both anatomically important and also have significant implications for the neuroendoscopic practice of traversing FoM when gaining access to the third ventricle to create third ventriculostomies, as well as in avoiding injury to adjacent anatomical structures during these endoscopic and open neurosurgical procedures. Knowledge of the precise morphometrics of FoM is important, to the extent that Nagm et al. (2016) have recommended the recording of the diameter of FoM for each patient enrolled in a neuroendoscopic procedure.

Clinical magnetic resonance imaging (MRI) could be used to better characterize the *in vivo* anatomy of FoM. However, use of routine neuroimaging would unfortunately be suboptimal in that regard because standard orthogonal MRI projections of the brain do not match the true anatomical spatial configurations of FoMs, thus depicting them in a falsely foreshortened and distorted manner. Here we investigate in detail the normal anatomic and morphometric features depicting size, shape, and angulation of FoMs when acquired in their true spatial orientation, using 3D high-resolution MRI. Based on our findings, we also propose a new name for this anatomical structure.

## MATERIALS AND METHODS

All imaging was performed during routine diagnostic neuroimaging work-up of consenting patients based on clinical indications. Retrospective access to anonymized imaging studies of these patients was approved for this research by our institutional research and development office. The requirements for individual patient consent and ethics review were waived since no prospective imaging of patients or volunteers was necessary. We retrospectively reviewed brain MR images of 100 patients aged 18-83 years (50% males, and 50% females) who had been imaged for various indications (most commonly headaches or a suspected cerebrovascular event) but whose imaging was subsequently determined by a neuroradiologist to be normal, allowing for commonly found non-specific white matter hyperintensities of presumed microvascular origin, and minimal age-appropriate degrees of global brain atrophy (we objectively accounted for this; see below).

We obtained the MRI scans on a 3T whole-body MR unit (Discovery MR750, GE Medical Systems, Milwaukee, Wisconsin) using a standard head coil with eight elements (8 HR Brain; GE Healthcare). All images were acquired using the same standardized brain protocol that included a 3D inversion recovery-prepared FSPGR (fast spoiled gradient echo) acquisition producing isotropic T1-weighted volumes at 1 mm resolution. These images were obtained with a repetition time/echo time [TR/TE] of 4.8/11.1 ms; slice thickness 1 mm; and an acquisition matrix of 416 × 256 pixels in the coronal plane.

An experienced neuroradiologist, blinded to the clinical data, initially viewed all retrospectively obtained anonymized 3D FSPGR images on a GE Healthcare Centricity PACS-IW review workstation. We imported these images into Osirix 10.0 (Pixmeo, Switzerland) and reviewed them using source images and multiplanar reformats at default window parameter settings. We then obtained volume-rendered (VR) images using the built in Osirix 3D VR capabilities. We electronically measured linear dimensions and angles between different anatomical structures on the images using the Osirix length and angle tools, respectively. All these morphometric measurements on images using electronic calipers were quantitative,

objective, and unambiguous, thus not requiring the measurement of intraobserver agreement (Viera and Garrett, 2005; Wikipedia contributors, 2019). Moreover, since there were no subjective, qualitative, or semi-qualitative recordings made in this study, that is, the measurements did not contain any ambiguity in the characteristics of interest in the rating target, it was also not necessary for more than one person to perform the measurements (Wikipedia contributors, 2019).

We first measured angulations of the true anatomical planes of FoMs relative to the orthogonal imaging planes aligned with the Talairach anterior commissure to posterior commissure line (AC-PC, spanning the superior aspect of the anterior commissure and inferior aspect of the posterior commissure), commonly used in standard neuroimaging and neuronavigation planning (Weiss et al., 2003). In particular, for each FoM we measured angulation of the superomedial border relative to the AC-PC line in the sagittal imaging plane; angulation of the anterior border of FoM relative to the midsagittal line in a coronal imaging plane perpendicular to AC-PC line; and angulation of the inferior border of FoM relative to the midsagittal line in an axial imaging plane parallel to the AC-PC line (see Results for a detailed description and illustrations).

Next, we measured the minimum width of FoM in its true anatomical double oblique plane, the thickness of the fornix forming the anterior border of the FoM as a measure of the 'depth' (or length) of the FoM, and the width of the fornix as a measure of the distance between the medial borders of FoMs on both sides. We also measured the width of the third ventricle at the level at which the forniceal columns enter the lateral walls of the third ventricle (see Results for further details and illustrations).

As an estimate of the degree of cerebral atrophy, we also obtained the Evans' index (EI) by dividing the maximum width between the frontal horns of the lateral ventricles and maximum internal diameter of the skull at the same axial level. Subjects exceeding normal population EI values for age according to Brix et al. (2017), that is, male/female: 65-69 years: 0.34/0.32; 70-74



years: 0.36/0.33; 75-79 years: 0.37/0.34; and 80-84 years: 0.37/0.36, were omitted from the analysis.

Owing to the nature of the measurements obtained over a range of different ages and the dependence of the measured parameters on age (see Results), most of the parameters (with exception of the width of the fornix) did not follow a normal distribution, and non-parametric testing was therefore used for statistical analysis. We first compared linear dimensions and angles between the right and left sides using a non-parametric *t*-test for dependent samples, and because we found no significant differences between both sides, we used average measurements from both sides for subsequent analysis. Similarly, since we found no significant differences between male and female subjects using a non-parametric Mann-Whitney U-test, we used pooled measurements for both sexes in the subsequent correlation analyses. We tested correlations between different parameters using a non-parametric Kendall's tau correlation measure, considered more robust than the Spearman's correlation test. We performed all analyses using SPSS 25.0 (IBM). The values of *P* less than 0.05 were considered statistically significant.

## RESULTS

### **Spatial Anatomic Relations and Dimensions of the Interventricular Foramen on Imaging**

In contrast to the original description by Monro, the right and left FoM were separate, distinct, and spatially oriented relative to each other in a V-shaped configuration, each one separately leading from each lateral ventricle into the antero-superior aspects of the third ventricle.

Each FoM was observed as a discrete round, oval, or crescent-shaped canal-like passage with well-defined superomedial, anterior and inferior borders formed by the semicircular concavity of the ipsilateral column of the fornix (**Fig 1**). The superomedial border of FoM was formed by the most anterior aspect of the body of the fornix as it separates into two forniceal columns at the level of the anterior margin of the thalamus. Rostral to this point, each column of the fornix courses inferiorly and laterally, outlining the anterior border of FoM, and just above the level of the anterior commissure also turns posteriorly, contributing to the inferior border of FoM (**Fig. 1**). This curvature of the fornix determines the anatomical plane of FoM, which is angled anteriorly and superiorly. The part of each FoM encircled by the column of the fornix resembles a short canal with a discrete depth equivalent to the thickness of the fornix, and walls shaped like an inner surface of a torus. The lateral and posterolateral aspects of FoM, defined by the genu of the internal capsule and the anterior convex surface of the thalamus, are less discrete and hyperboloid in shape, although curvature of the anterior tubercle of the thalamus and its ependymal lining contribute to the perceived shape of the foramen. Posteriorly, each FoM merges with the choroid fissure, a narrow cleft between the fornix superolaterally and thalamus inferomedially, enclosed by the choroid plexus and tela choroidea plus a network of associated veins and arteries. FoM can therefore be considered as the most anterior, widened part of the choroid fissure devoid of the vascular structures, and its posterior margin is anatomically rather poorly defined other than by the presence of the choroid plexus passing from each lateral ventricle to third ventricle, and the thalamostriate vein which often crosses through the posterior margin of FoM (**Fig. 1**).

Given the complex spatial relationships of each FoM, it is difficult to translate 3D images as seen on a cadaveric specimen or neuroendoscopy into planar 2D imaging appearances. Owing to the obliquity of the anatomical planes of FoM in relation to the typical orthogonal imaging planes, the true angulation of FoM differs from that perceived on standard coronal or axial brain MR images, and it is difficult to estimate the diameter of FoM on such conventional images, because the distance to be measured is not contained in one imaging plane. For example, it is easy to mistake the inferior part of the frontal horn of the lateral ventricle as the site of FoM, especially in narrow ventricles where each frontal horn tapers into a funnel-shaped conduit, and to erroneously assume that the narrowest part of this conduit represents FoM itself (**Fig. 2A**). In a more posterior coronal plane it is also possible to mistake the choroid fissure for FoM, since the structures forming their borders (that is, the fornix and thalamus) are similar (**Fig 2B**).

To describe the true anatomy of FoM, we measured angulation of the borders of each FoM in relation to the orthogonal planes when adjusted relative to the AC-PC line. In particular, we first measured (relative to the AC-PC line) the angulation of the superomedial border of FoM formed by the anterior aspect of the body of the fornix as it splits into the two columns (**Fig. 3A-D**). We then established the angulation of the anterior border of FoM formed by the column of the fornix diverging laterally from the midsagittal line, measured in the coronal imaging plane intersecting the anterior aspect of the fornix, and expressed in relation to the midsagittal line (**Fig. 3E**). Finally, we measured the lateral angulation, relative to the midsagittal line, in the axial imaging plane of the inferior border of FoM partially outlined by the column of the fornix, which turns posteriorly above the anterior commissure to enter the wall of the third ventricle behind the anterior commissure (**Fig 3F**).

The values we obtained for the measured parameters are presented in **Table 1**. The mean angulations of the planes of FoM as defined by the angulation of its superomedial, anterior, and inferior borders were  $56.8^\circ \pm 9.1^\circ$  superiorly from the axial plane,  $22.5^\circ \pm 10.7^\circ$  laterally from the midsagittal plane, and  $37.0^\circ \pm 6.9^\circ$  from the midsagittal plane, respectively. The axis of FoM itself,

that is, the line or path along which a linear object such as an endoscope would need to pass perpendicular to the plane of FoM, would therefore be angled on average at 33.2° superior to the axial plane or AC-PC line (by looking in the sagittal imaging plane), 67.5° lateral to the midsagittal line (by looking in the coronal imaging plane), and 53.0° anterior to the midsagittal plane (by looking in the axial imaging plane), respectively.

In addition, we measured the width of the fornix as a measure of the distance between the medial borders of FoM on each side (**Fig. 3B**), thickness of the column of fornix as a measure of the 'depth' of the FoM (**Fig. 3E**), and the maximum width of the third ventricle at the level at which the columns of the fornix enter the wall of the ventricle (**Fig. 3F**). To measure the true width of each FoM we obtained double oblique projections through its anatomical plane angled along the inferior and anterior border of FoM (**Fig. 4A-B**). In this projection FoM was seen *en face* partially encircled by the fornix (**Fig. 4C**). The minimum width of FoM in all subjects was perpendicular to the superomedial border of the foramen. The choroid plexus was poorly defined and, in most cases, it was not possible to reliably establish the posterior border of the FoM and measure the corresponding diameter.

There were no significant differences in any of the dimensions between male and female subjects (**Table 1**). The mean minimum diameter of FoM was  $2.8 \pm 1.2$  mm (range 1.2-5.8 mm), while the depth (length) of FoM was  $2.5 \pm 0.2$  mm (1.9-3.1 mm). Additionally, we demonstrated FoMs on volume rendered (VR) virtual reality projections (**Fig. 5**) but did not use these images for morphometric measurements (see Discussion).

### **Changes in Dimensions and Angulation of the Interventricular Foramen with Age and Evans' Index**

The minimum diameter of FoM significantly increased with age (**Table 2, Fig. 6A**), as well as with substitute measures of brain atrophy such as the EI or width of the third ventricle (**Table 2**). However, the depth of FoM, as determined by the thickness of the forniceal column, remained

relatively constant (**Fig. 6B**). As a result, in young subjects, FoM had a diameter smaller than the depth, a configuration perhaps better described as a short canal, or canaliculus. The ratio of the depth to diameter progressively diminished with age (**Fig. 6C**), and the minimum diameter of FoM became larger than its depth in most subjects over 50 years of age.

With increasing age, there were also significant changes in the angulations of the anatomical planes of FoM (**Table 2, Fig. 6D-F, and Fig. 7**). In a young individual, the angle of the superomedial border to AC-PC line was large, reflecting a near vertical direction of travel of the forniceal column in the sagittal plane, as well as in the coronal plane, as shown by the low lateral angulation of its anterior border in the coronal plane from the midsagittal line. Angulation of the inferior border from the midsagittal line in the axial plane was also low. As a result, the orientation of FoM in young subjects was nearly in the sagittal plane. As the minimum diameter of FoM was perpendicular to its superomedial border (body of fornix), and the foramen was oval in shape, the lumen of FoM was oriented almost vertically (**Fig 7**). With age, the diameter of FoM increased, the fornix became flatter and the angulation of FoM to the axial plane diminished. The anterior and inferior borders of FoM angled away from the midsagittal line (**Fig. 7**), resulting in a more horizontal lie of FoM, with some lateral and anterior angulation. This is a configuration that is much more amenable to easy traversal of the foramen during standard neuroendoscopic approaches, for example en route to the floor of the third ventricle from initial entry at the frontal horn of the lateral ventricle.

## **DISCUSSION**

Alexander *Monro secundus* (1733-1817) was an extraordinary anatomist and a successful lecturer, having held the Chair of Medicine, Anatomy, and Surgery at the University of Edinburgh for almost five decades of his academic career (Sharp, 1961; Wu et al., 2012; Tubbs et al., 2014; Patel et al., 2018). His most significant works included the anatomic descriptions of the interventricular foramen, and of the physiological *Monro-Kellie* doctrine. Accordingly, he made invaluable contributions to neuroanatomy and neurophysiology, with lasting impact on contemporary clinical neurosciences. Much of the history surrounding the anatomic description of FoM was previously reviewed by Sharp (1961), and is summarized herein.

Although a number of anatomists had identified the presence of a short conduit between the paired lateral ventricles and the third ventricle of the brain (or had appreciated in general a similar communication) before *Monro*, he was the first to describe in detail and to provide the clearest illustration of the foramen that we today call the FoM (*Monro*, 1783). That said, while many credit *Monro* with the discovery of the interventricular foramen, he acknowledged at that same time that other anatomists were aware of its existence before him, stating that “These cavities have been described by *Galen*, and by many succeeding authors of eminence, as all communicating with each other.” Thus, according to Sharp (1961), *Monro* was perfectly honest in pointing out at the outset that the presence of a communication between the ventricles was already well known, but *Monro* suggested that: (1) it had not been illustrated before his time, (2) others may have cast some doubt about its presence, and (3) some workers had entirely overlooked or denied its existence. The general impression gained from *Monro*'s work is that no description of the communication prior to his own account was of any value (Sharp, 1961).

### **Anatomical Description of the Interventricular Foramen before *Monro***

The first known anatomic drawings of the foramen were illustrated by *Leonardo da Vinci* in the 1510's and were based on a wax cast of the ventricles of an ox brain (Patel et al., 2018). These

drawings demonstrated a clear communication between each lateral ventricle and the third ventricle.

Andreas Vesalius (1514-1564) also mentioned the interventricular foramen, first in his *Fabrica* and subsequently in his *Epitome*. There, he describes: “The lower regions of the ventricles...are not partitioned from each other by the septum but come together in a sinus (the third ventricle) lying under the body formed like an arch (fornix); this space extends directly downwards as a prominent channel through the substance of the brain into a funnel or basin formed by a thin membrane of that shape (the infundibular recess).” Vesalius probably had the correct idea that the lateral ventricles and third ventricle indeed had a communication but he was inaccurate in his descriptions. Adrian van der Spigelius (1578-1625) in his writings offered no new knowledge on the earlier descriptions by Vesalius (Wu et al., 2012).

In 1682 Thomas Willis also provided a similar account to that of Vesalius. He stated that: “Into this (third) ventricle there are two openings, one of which stands in the beginning of it and the other at its end; and through the middle of its extent a downward sloping aperture stretches toward the infundibulum, so that a serous humour coming up to or other of the foramina flows down immediately to the infundibulum.” Jacob B. Winslow in 1732 also described: “The infundibulum opens above immediately before the optic thalami, by the oval hole named foramen commune anterius, and consequently communicates with the lateral ventricles.” Haller in 1776 also wrote about the communication between the lateral and third ventricles, but in an “ambiguous” manner, according to Sharp (1961).

### **Anatomical Description of the Interventricular Foramen by Monro**

Monro first described the interventricular foramen at a meeting of the Philosophical Society of Edinburgh in 1764, during which he gave detailed illustrations of FoM and its pathological changes in the setting of hydrocephalus. This was evident from an autopsy of a 3-year-old boy performed

by Monro and his colleague Robert Whytt (1714-1766) in 1753. The boy had suffered from hydrocephalus, and the foramen appeared enlarged on dissection (Sharp, 1961).

In 1783 Monro published about the FoM in a paper titled *Observations on the Structure and Functions of the Nervous System*, stating: "After laying open one of the lateral ventricles of the brain in the usual way, leaving the septum between the ventricles entire, let the gutter which is between the corpora striate and thalami nervorum opticorum, the bottom of which is occupied by the substance called Centrum semicirculare geminum, be traced inwards, and it will be found to lead to the fore part of an oval hole, large enough to admit a goose quill, under the fore part of the fornix. From this hole, a probe can readily be passed into the other lateral ventricle, shewing, in the first place that the two lateral ventricles communicate with each other. When the fornix is next divided transversely, we find that this passage has the anterior crura of the fornix in the fore part, and the joining or middle part of the choroid plexus of the lateral ventricles at its back part, and that its middle part is over a passage downwards, named the iter ad infundibulum, or vulva, which should rather be called iter ad tertium ventriculum." Fourteen years later (1797), Monro published these same observations again in his *Treatise on the Brain*.

Thus, Monro mistakenly believed the interventricular foramina were part of a T-shaped communication, where they were each positioned at either end of a transversely directed passage, constituting a direct connection between the two lateral ventricles, and which, in turn, opens inferiorly into the third ventricle via a vertically disposed orifice that he referred to as the "iter ad tertium ventriculum" (Monro, 1783; Sharp, 1961).

### **Disputes Regarding the Anatomy of the Interventricular Foramen at the Time of Monro**

It appears that Monro's first account of the FoM did not receive general approval. Monro thought it necessary therefore to repeat his 1783 beliefs again in his 1797 *Treatise on the Brain*, and to comment: "To my very great surprise, however, I have been informed, that several Teachers of Anatomy in London have told their Pupils, that they had looked for such passages in vain; and



therefore ventured to deny their existence.” Monro was so determined to vindicate himself and dispel any doubts about his description of FoM to the extent that he appended a “Declaration by the Professors of the Faculty of Physic in the University of Edinburgh” which ends: “We therefore entertain no doubt of the existence of the communication of the Lateral Ventricles of the Brain with each other, and with The Third Ventricle, described by Dr Monro in the work he published on the Nervous System in 1783” (Sharp, 1961).

Clearly, the passage of 14 years had not changed Monro's views. Despite the opposition to his statements, there were no published denials or rebuttals. According to Sharp (1961), it would seem that the 'Teachers of Anatomy in London' were fully aware of the continuity between the lateral and third ventricles, but simply did not agree with Monro's interpretation. Such opposed viewpoints could well have been owing to different methods of brain dissection.

Alexander Monro secundus retired in 1798, 54 years after his appointment. In 1802, however, there was one episode of hostile criticism of Monro. This was a personal attack on him by Sir Charles Bell for presuming to describe an anatomic structure that had already been well known, rather than an attempt to show that his description was misleading. It can be found as an appendix to a series of engravings of the brain by Bell. The details of Bell's grievance are laid out succinctly by Sharp (1961), but the overall gist of it was that Bell believed Monro had given a false idea of the extent and accuracy of already existing knowledge and considerably accurate work that had been published long before Monro's time, to publicize Monro's own observations at the expense of these prior descriptions.

### **More Accurate Descriptions of the Communications between the Lateral and Third Ventricles since Monro**

The true relationship of the communications between the lateral and third ventricles was most accurately depicted by means of plastic casts of their cavities. Both Retzius (1900) and, more recently, Last and Tompsett (1953) had used this plastic injection technique to produce excellent

casts. Sharp (1961) summarized his descriptions and communications based on these casts, as follows: “The lateral ventricle is connected to the third ventricle by a short thick stalk of resin, representing the interventricular foramen. The stalks of the two sides are symmetrical, diverging slightly upwards from the side walls of the third ventricle just behind the notch made by the anterior commissure. The two stalks are joined, separately from each other, to the right and left walls of the body of the third ventricle, the roof of which projects upwards as a sharp ridge between them.”

### **Three-Dimensional Spatial Configuration of the Interventricular Foramen Based on Multiplanar MRI Morphometry**

We here provide the first detailed description of *in vivo* MRI morphometric features for FoM, and show that: (1) FoMs are two in number, oriented relative to each other in a V-shaped configuration; (2) their true sizes and orientations differ from those perceived on standard MR images of the brain; and (3) each FoM often has a 3D spatial configuration resembling a short narrow canal, especially in the young, but it dilates above the age of 50 years.

It was feasible for us to obtain VR images from standard imaging datasets. Rendered images allowed a good general overview of the angulation and position of each FoM but in our opinion they are unreliable for measurements of linear dimensions, as the sizes of rendered FoMs greatly change depending on the windowing used in the 3D rendering algorithm (**Fig. 5**). While windowing also affects 2D planar images, the effect is minimal and much less pronounced than for 3D VR images. As such, we believe that recent work attempting to measure FoM size based on VR images and reconstructions may be less reliable (Jean et al., 2019).

Our anatomic study has several implications for the neuroendoscopic practice of traversing FoM to gain access to the third ventricle, e.g. to perform third ventriculostomies. First, the correct orientation for traversing FoM using a standard approach is usually not too difficult to establish by first identifying the relative positions of anatomical structures such as FoM, septal veins, thalamostriate veins, and the choroid plexus (Jung et al., 2017). However, our findings

have important practical significance in that we show that traversing FoM using a 'standard' trajectory in a young person would likely be difficult and unsafe, since FoM is a vertical fissure-like opening oriented almost in the sagittal plane. In these cases, a steeper endoscopic approach to FoM may be used along with other considerations of ventricular size to determine optimal trajectories for these procedures, as discussed by Zador et al. (2017) previously. Second, according to Nagm et al. (2016), most, if not all patients without hydrocephalus would be expected to have a "normal to small FoM" with a vulnerability to unilateral forniceal damage during passage of an endoscope through FoM. However we convincingly demonstrate that the width of FoM is age-dependent, and that its traversal by an endoscope would theoretically be easier in the over-50 age group. Lastly, endoscopic third ventriculostomy can be regarded as a low-complication procedure, but, nonetheless, transient and permanent morbidities can occur (Bouras et al., 2011). With regard to passage of an endoscope through FoM, major bleeding may occur following injury to branches of the septal and thalamostriate veins. Laceration may also affect the choroid plexus. Moreover, intraoperative mild contusion of the ipsilateral fornix during passage through FoM is well known. For instance, this occurred in five out of 94 cases in one series by Kehler et al. (2003), but only in 0.04% of patients in another series reported by Bouras et al. (2011). This type of injury does not usually cause memory disturbances unless a contralateral endoscopic procedure is performed within a short period of prior damage to one fornix (Jung et al., 2017). However, permanent memory loss may still occur after any forniceal injury (Bouras et al., 2011). Of note, the genu of the internal capsule touches the wall of the third ventricle in the area lateral to FoM near the anterior pole of the thalamus (Rhoton, 2002), and we know that injury to the internal capsule may result in hemiparesis. This may explain the mechanism for observed transient and permanent hemiparesis occurring in 0.34% of cases after endoscopic third ventriculostomy (Boras et al. 2011).

## **Conclusions and Proposed New Terminology**

In 1961, Sharp (1961) aptly summarized the extent of Monro's error in his original description of FoM. Sharp (1961) rightly pointed out that the two FoMs in fact do not join each other to make a transverse canal. Theoretically, it might be possible to pass a maleable or pre-shaped probe, but most unlikely a rigid probe or a "goose quill" (Monro, 1783), from one lateral ventricle, through its FoM, and back into the equivalent contralateral foramen, but only by crossing the cavity of the third ventricle first. Monro mistakenly described a third foramen leading from the supposed transverse passage joining FoMs into the roof of the third ventricle just behind the anterior pillars of the fornix (Monro, 1783). Thus, the retention of the eponymous term 'foramen of Monro' as a synonym for the interventricular foramen would therefore seem unjustified for two reasons, as also stated by others: first, because Monro would seem to have added nothing of value to the pre-existing descriptions of the foramen; and second, because he actually misinterpreted or misrepresented the nature of the communication between the third and lateral ventricles. Indeed, FoM has been labeled as a misnomer previously (Sharp, 1961; Sarwar, 1977; Cai et al., 2015). Sarwar (1977) also concurred with the notion of abandoning the term FoM, and indeed, the 1998 Terminologia Anatomica does not mention FoM but only uses 'interventricular foramen'.

We provide a comprehensive and detailed description of the spatial anatomic and morphometric features for the two interventricular foramina as seen on *in vivo* high-resolution multiplanar MRI, and show that, up to the age of about 50 years, they are in fact frequently shaped as short canals measuring under 3 mm in length, and, less so, in width. Therefore, to avoid the furtherance of confusion about the anatomy (number, size, shape, and spatial orientation) of these structures, as well as their terminology (questionable ascription to Monro, and whether they are 'foramina'), we here repeat the proposal by others that not only the eponym 'Monro' should no longer be associated with this structure, but we also add that the term 'foramen' be abandoned henceforth. Instead, we propose that each unilateral anatomical structure be re-named as the 'interventricular canaliculus', or 'IVC' for short. Our analysis and measurements depict this configuration in individuals under the age of 50 years. This shape is also reminiscent of the 'stalks

of resin' described previously on casts of ventricles by Retzius (1900) and Last and Tompsett (1953). This new terminology also avoids confusion with the embryological primary interventricular foramen of the heart. Our detailed description of the spatial configuration and morphometry of these proposed newly named IVCs, derived from analysis of *in vivo* 3D MR imaging datasets, should put to rest any further misconceptions and confusions regarding their anatomy, and should be useful in accurate descriptions of their neuroimaging findings and in precise planning of safer neuroendoscopic and neurosurgical procedures centered on this region.

**Conflict of Interest**

The authors declare no conflict of interest

**Acknowledgements**

none

## REFERENCES

- anatomyEXPERT. 2019. Interventricular foramen. URL: <http://www.anatomyexpert.com/app/structure/6197/22250/> [accessed Dec. 14, 2019].
- Bouras T, Sgouros S. 2011. Complications of endoscopic third ventriculostomy. *J Neurosurg Pediatr* 7:643-649.
- Brix MK, Westman E, Simmons A, Ringstad GA, Eide PK, Wagner-Larsen K, Page CM, Vitelli V, Beyer MK. 2017. The Evans' Index revisited: New cut-off levels for use in radiological assessment of ventricular enlargement in the elderly. *Eur J Radiol* 95:28-32.
- Cai Q, Wang J, Wang L, Deng G, Chen Q, Chen Z. 2015. A classification of lesions around interventricular foramen and its clinical value. *Int J Clin Exp Pathol* 8:9950-9957.
- Glastonbury CM, Osborn AG, Salzman KL. 2011. Masses and malformations of the third ventricle: normal anatomic relationships and differential diagnoses. *Radiographics* 31:1889-1905.
- Harisinghani MG, Chen JW, Weissleder R. 2011. Neurologic Imaging. In: *Primer of Diagnostic Imaging*. In: Philadelphia: Elsevier. p 353-362.
- Jean WC, Tai AX, Hogan E, Herur-Raman A, Felbaum DR, Leonardo J, Syed HR. 2019. An anatomical study of the foramen of Monro: implications in management of pineal tumors presenting with hydrocephalus. *Acta Neurochir (Wien)* 161:975-983.
- Jung TY, Chong S, Kim IY, Lee JY, Phi JH, Kim SK, Kim JH, Wang KC. 2017. Prevention of complications in endoscopic third ventriculostomy. *J Korean Neurosurg Soc* 60:282-288.
- Kehler U, Regelsberger J, Gliemroth J. 2003. The mechanism of fornix lesions in 3rd ventriculostomy. *Minim Invasive Neurosurg* 46:202-204.
- Last RJ, Tompsett DH. 1953. Casts of the cerebral ventricles. *Br J Surg* 1953 40:525-543.
- Monro A. 1783. Observations on the structure and function of the nervous system. Edinburgh. DOI: <https://doi.org/10.11588/diglit.4812>.
- Nagm A, Ogiwara T, Goto T, Chiba A, Hongo K. 2016. Neuroendoscopy via an extremely narrow foramen of Monro: A case report. *NMC Case Rep J* 4:37-42.

- Patel K, Mishra P, Choudhari KA. 2018. Commentary: Alexander Monro of "The foramen of Monro". *Neurosurgery* 83:E146-E152.
- Raybaud C. 2018. Radiology of hydrocephalus. In: Cinalli G., Ozek M., Sainte-Rose C. (eds) *Pediatric Hydrocephalus*. Cham: Springer.
- Retzius G. 1900. The shape of the human brain ventricles after casting. *Biol Untersuch* 9:45.
- Rhoton AL Jr. 2002. The lateral and third ventricles. *Neurosurgery* 51(4 Suppl):S207-271.
- Sharp JA. 1961. Alexander Monro secundus and the interventricular foramen. *Med Hist* 5:83-89.
- Thorek P. 1985. Ventricular system and cerebrospinal fluid. In: Thorek P. *Anatomy in Surgery*. New York: Springer-Verlag. p 39-40.
- Tubbs RS, Oakes P, Maran IS, Salib C, Loukas M. 2014. The foramen of Monro: a review of its anatomy, history, pathology, and surgery. *Childs Nerv Syst* 30:1645-1649.
- Viera AJ, Garrett JM. 2005. Understanding interobserver agreement: The kappa statistic. *Fam Med* 37:360-363.
- Weiss KL, Pan H, Storrs J, Strub W, Weiss JL, Jia L, Eldevik OP. 2003. Clinical brain MR imaging prescriptions in Talairach space: technologist- and computer-driven methods. *AJNR Am J Neuroradiol* 24:922-929.
- Wikipedia contributors. (2019). Inter-rater reliability. In Wikipedia, The Free Encyclopedia. Retrieved December 14, 2019, from [https://en.wikipedia.org/w/index.php?title=Inter-rater\\_reliability&oldid=881644428](https://en.wikipedia.org/w/index.php?title=Inter-rater_reliability&oldid=881644428)
- Wilder BG. 1880. The foramina of Monro: some questions of anatomical history. [Accessed online through <http://www.NEJM.org/>.] *Boston Med Surg J* 103:152–154.
- Woollam DH, Millen JW. 1953. Anatomical considerations in the pathology of stenosis of the cerebral aqueduct. *Brain* 76:104-112.
- Wu OC, Manjila S, Malakooti N, Cohen AR. 2012. The remarkable medical lineage of the Monro family: contributions of Alexander primus, secundus, and tertius. *J Neurosurg* 116:1337-1346.

Zador Z, Coope DJ, Mostofi A, Kamaly-Asl ID. 2017. Operative planning aid for optimal endoscopic third ventriculostomy entry points in pediatric cases. Childs Nerv Syst 2017 33:269-273.



## FIGURE LEGENDS

### Figure 1

Anatomy of FoM on a cadaveric brain preparation, modified from Rhoton (2002), with permission. The superomedial border of FoM (white arrowhead) is formed by the most anterior aspect of the body of the fornix (F) as it separates into two columns (Fc) at the level of the anterior margin of the thalamus (T). The anterior border of FoM (gray arrowhead) is formed by the column of the fornix traveling inferiorly and diverging laterally; just above the level of the anterior commissure (AC) the column of the fornix turns posteriorly, contributing to the inferior border of FoM (black arrowhead). Choroid plexus (CP) traverses the posterior aspect of FoM. Thalamostriate vein (TSV); Corpus callosum (CC); Optic chiasm (OC).

### Figure 2

The region of FoM (panel **A**) and the anterior aspect of the choroid fissure (panel **B**) as seen on typical coronal images reconstructed parallel to the brainstem and the posterior commissural-obex line (PC-OB). (**A**) The diameter (small dimension bar) of the passage between the body of the fornix (F) and the genu of the internal capsule (IC) does not represent the true minimal diameter of FoM, which cannot be accurately depicted in this plane. The perceived axis of this passage (i.e., the solid arrow) varies substantially from the true anatomical axis of FoM in the coronal plane (dotted arrow), which depends on the course of the anterior aspect of the forniceal column, not seen in this plane. (**B**) On an image obtained more posteriorly, the choroid fissure can appear similar to the FoM. The presence of choroid plexus (arrow) may help recognise that the image has been obtained at the level of the choroid fissure, but the choroid plexus may not always be visible, and in narrow vertically-oriented foramina it may be visible in all coronal imaging planes. T: anterior pole of the thalamus.

### Figure 3

Measuring the angulation of the anatomical plane of FoM on axial, coronal and sagittal images, as labeled on each panel. Angulation of the superomedial border of FoM (formed by the body of the fornix as it splits into the columns) was measured by finding a point abutting the posterior margin of the fornix in the axial plane (**A**, white dot) and its inferior margin in the coronal plane (**B**, white dot), and drawing a line through this point tangential to the posterior surface of the fornix in the midsagittal imaging plane (dotted line in **C**). An angle between this line and the AC-PC line was taken as the angulation of the superomedial border of the FoM. Moving laterally to the parasagittal plane (**D**) confirms that the dotted line established in (**C**) lies in the plane of FoM between the column of the fornix turning laterally (white arrowhead) and faintly visible choroid plexus (black arrowhead). We also measured the width of the fornix (dimension bar in **B**) as the distance between the medial borders of the two FoMs. (**E**) Angulation of the anterior border of FoM formed by the columns of fornix diverging laterally (dotted line) was measured in relation to the midsagittal line (solid line) in the coronal imaging plane that intersects the columns of fornix. We measured the thickness of the column of the fornix at its mid length as the 'length' of FoM (dimension bar in **E**). (**F**) The inferior border of FoM is partially outlined by the column of fornix as it turns posteriorly above the anterior commissure and enters the wall of the third ventricle (3V) behind the anterior commissure (AC) traveling towards the mammillary body. Owing to a curvilinear direction of travel of this part of the forniceal column, its projection onto the axial imaging plane was established by scrolling through the axial image stack and finding the line connecting the point at which the column of the fornix starts to curve laterally (inset) and the point at which it has entered the wall of the third ventricle (white arrowheads). We measured the anterior angulation of this line (dotted line) in relation to the midsagittal line (solid line). We also measured the maximum width of the third ventricle (3V) at this level (dimension bar in **F**).

#### Figure 4

Reconstructed images to demonstrate FoM in its true anatomical plane achieved by double angulation of the imaging plane, first along the inferior border of FoM in the axial plane (**A**, established as described in Figure 3F) and then along the anterior border of FoM in the resulting oblique coronal plane (**B**). (**C**) FoM (asterisk) is well demonstrated in this double oblique anatomical plane, encircled by the fornix at its superomedial (white arrowhead), anterior (gray arrowhead) and inferior border (black arrowhead) as it passes the anterior commissure (AC), with the remainder of the outline completed by the genu of the internal capsule (IC) and the anterior pole of the thalamus. Continuity of FoM with the choroid fissure posteriorly is seen clearly. The minimum diameter of FoM was always perpendicular to the superomedial border. The choroid plexus (CP) was poorly seen in most cases, making it difficult to reliably establish the posterior border of FoM.

#### Figure 5

Demonstration of FoM on volume rendered (VR) virtual reality projections. Examples of anterior (**A**) and oblique lateral (**B**) views with structures in the third ventricle erased to allow better demonstration of FoMs on a black background. While useful for general orientation, VR images are not suitable for measurements of linear dimensions which can vary greatly depending on image windowing (compare the apparent size of FoM in the main panel (B) obtained at a window level and width of 340/150 vs. the inset showing the same image at 250/100), as well as the contrast and brightness of the original images.

**Figure 6**

Changes in morphometric parameters of FoMs with age. **(A)** Diameter but not **(B)** depth of FoM increases with age. **(C)** Depth of FoM is larger than its minimum diameter up to approximately 50 years of age. **(D-F)** Changes in angulation of FoM with age.

**Figure 7**

Changes in appearances of the FoM with age. Examples from 18, 41 and 80 year-old individuals demonstrating that with age the FoM adopts a more horizontal and anteriorly angled position due to flattening of the fornix and changes in angulation of its anterior and inferior borders, as seen on sagittal coronal, and axial images (panels from top to bottom), and VR images.

## TABLES

**Table 1**

The sex distribution of mean values  $\pm$  standard deviations, and ranges (in parentheses) of morphometric measurements of FoMs. No statistically significant differences were observed between male and female subjects.

	<b>All Patients (n = 100)</b>	<b>Male (n = 50)</b>	<b>Female (n = 50)</b>
<b>Age (years)</b>	51.1 $\pm$ 21.1 (18-83)	51.8 $\pm$ 20.1 (18-82)	50.4 $\pm$ 22.2 (18-83)
<b>Evans' Index</b>	0.25 $\pm$ 0.03 (0.2-0.35)	0.26 $\pm$ 0.03 (0.2-0.35)	0.25 $\pm$ 0.03 (0.2-0.33)
<b>Minimum diameter (mm)</b>	2.8 $\pm$ 1.2 (1.2-5.8)	2.9 $\pm$ 1.2 (1.3-5.8)	2.7 $\pm$ 1.1 (1.2-5.4)
<b>Depth (mm)</b>	2.5 $\pm$ 0.2 (1.9-3.1)	2.6 $\pm$ 0.2 (2.2-2.9)	2.5 $\pm$ 0.2 (1.9-3.1)
<b>Width of the fornix (mm)</b>	4.7 $\pm$ 0.5 (3.6-6.1)	4.8 $\pm$ 0.5 (3.7-6.1)	4.6 $\pm$ 0.5 (3.6-5.8)
<b>Width of the third ventricle (mm)</b>	5.1 $\pm$ 2.3 (2.0-11.3)	5.6 $\pm$ 2.5 (2.0-11.3)	4.7 $\pm$ 1.9 (2.0-9.2)
<b>Angle of the plane of FoM (°)</b>			
<b>Superomedial border vs. axial plane</b>	56.8 $\pm$ 9.1 (41-80)	57.1 $\pm$ 9.1 (42-79)	56.6 $\pm$ 9.3 (41-80)
<b>Anterior border vs. midsagittal plane</b>	22.5 $\pm$ 10.7 (6-46)	23.4 $\pm$ 11.5 (6-46)	21.1 $\pm$ 9.7 (7-39)
<b>Inferior border vs. midsagittal plane</b>	37.0 $\pm$ 6.9 (16-51)	37.8 $\pm$ 6.8 (21-51)	36.2 $\pm$ 7.1 (16-50)

**Table 2**

Values of the Kendall's tau correlation coefficient ( $t$ ) between patient age, Evans' index, width of the third ventricle (width 3V), and the dependent variables (dimensions and angles of FoM).

Statistically significant correlations are shown in brackets.

	<b>Age</b>	<b>Evans' index</b>	<b>Width 3V</b>
<b>Diameter (mm)</b>	[0.677] **	[0.524] **	[0.675] **
<b>Depth (mm)</b>	0.118 ns	0.126 ns	0.127 ns
<b>Width of the fornix (mm)</b>	-0.009 ns	0.110 ns	0.071 ns
<b>Angle</b>			
<b>Superomedial border vs. axial</b>	[-0.456] **	[-0.337] **	[-0.431] **
<b>Anterior border vs. midsagittal</b>	[0.645] **	[0.551] **	[0.678] **
<b>Inferior border vs. midsagittal</b>	[0.471] **	[0.434] **	[0.463] **
<b>Age vs. Evans' index</b>	[0.424] **		
<b>Age vs. width 3V</b>	[0.600] **		
<b>Evans' index vs. width 3V</b>	[0.511] **		

\*\* :  $P < 0.05$  (two-tailed); ns: not significant.