Maria Agnese Pirozzi

Tutor: Prof. Mario Cesarelli

co-Tutors: Dr. Mario Quarantelli, Ing. Mario Magliulo

Innovative Techniques to Devise 3D-printed Anatomical Brain Phantoms for Morpho-functional Medical Imaging

Università degli Studi di Napoli Federico II

Institute of Biostructures and Bioimaging

My Background

My education & training

Graduation

M.Sc. degree cum laude in *Biomedical Engineering* from the University of Naples "Federico II" on January 31, 2017.

Fellowship

- PhD Student of XXXIII cycle in Information Technology and Electrical Engineering (ITEE), part of BioMedical Engineering Group of the Department of Electrical Engineering and Information Technology (DIETI) of University of Naples "Federico II" *without fellowship*.
- Grantee of a *research fellowship* at the National Research Council of Italy – Institute of Biostructure and Bioimaging (CNR-IBB) since April 2017.

Experience abroad

4 months at Reykjavik University, School of Technology, Department of Engineering, Medical Technology Center, Iceland.

BME DIETI UNINA

National Research Council of Italy

ibb Institute of Biostructures and Bioimaging

HÁSKÓLINN Í REYKJAVÍK
REYKJAVIK UNIVERSITY

Credits summary

Training plan

Module title	Year	Type	Credits	Certification
Biomedical Imaging	1	*MSc Module*	6	x
Computer Interface for Biological Systems (CIBS)	1	*MSc Module*	6	x
Green Economy and Managment in Engineering Projects	1	*Ad-hoc Module*	3	x
Morphic Sensing	1	*Ad-hoc Module*	2,4	x
How to publish a scientific paper	1	*Research Enhancement*	0,4	x
SIE2018 PhD School	1	*PhD School*	4	x
Data Science and Optimization	2	*Ad-hoc Module*	1,2	x
Machine Learning	2	*Ad-hoc Module*	5	x
New directions in biomedical engineering research: neuroscience, machine learning and personalised medicine	2	*Ad-hoc Module*	2	x
True Unipolar Electrocardiography and Application to Medicine	2	*Ad-hoc Module*	2,4	x
Applied Statistics and Research Methodology for Medical and Social Sciences	3	*External Course*	4,8	x

Seminar title	Year	Type	Credits	Certification
From medical imaging to surgical planning: new directions for Bone and Muscle Assessment	1	*Seminar*	0,4	x
Using electroencephalography (EEG) to investigate the role of neocortical brain in postural control and postural adaptation when exposed to vibratory proprioceptive stimulation	1	*Seminar*	0,4	x
XXXVII Annual School of Bioengineering organized by the Italian National Bioengineering Group (GNB)	1	*PhD School*	5	x
Parallel and distributed computing with Matlab	1	*Seminar*	0,4	x
Network Analysis, Data Science and Control in Computational Neuroscience	1	*Seminar*	0,2	x
Medical Thermal Therapy and Monitoring usinc Microwave Inverse Scattering	2	*Seminar*	0,2	x
XXXVIII Annual School of Bioengineering organized by the Italian National Bioengineering Group (GNB)	2	*PhD School*	5	x
How to get published with IEEE	3	*Seminar*	0,4	x
BCI & Neurotechnology Spring School	3	*Spring School*	5	x
Challenges and opportunity of medical imaging in the era of big data	3	*Seminar*	0,4	x

Credits summary

Credits per year

Student: Maria Agnese Pirozzi mariaagnese.pirozzi@unina.it
Tutor: Mario Cesarelli cesarell@unina.it
Co-tutors: Mario Quarantelli, Mario Magliulo quarante@unina.it mario.magliulo@ibb.cnr.it
Cycle XXXIII

	Credits year 1								Credits year 2								Credits year 3										
	Estimated	1 bimonth	2 bimonth	3 bimonth	4 bimonth	5 bimonth	6 bimonth	Summary	Estimated	1 bimonth	2 bimonth	3 bimonth	4 bimonth	5 bimonth	6 bimonth	Summary	Estimated	1 bimonth	2 bimonth	3 bimonth	4 bimonth	5 bimonth	6 bimonth	7 bimonth*	Summary	Total	Check
Modules	22	0	0	7	8,4	6	0,4	**22**	10	1,2	0	7	2,4	0	0	**11**	5	0	0	0	0	0	4,8	0	**4,8**	**37**	30-70
Seminars	6	0	0	0,8	0	5	0,6	**6,4**	5	0	0	0,2	0	5	0	**5,2**	5	0	5,4	0	0,4	0	0	0	**5,8**	**17**	10-30
Research	32	8	8	2,2	1,6	3	9	**32**	45	7	11	2,2	4	8	12	**44**	50	10	4	5	5	10	5	10	**49**	**125**	80-140
	60	8	8	10	10	14	10	**60**	60	8,2	11	9,4	6,4	13	12	**60**	60	10	9,4	5	5,4	10	9,8	10	**60**	**180**	180

*request for a two-month extension of the PhD program, as per D.L. n. 34 del 19/05/2020, art. 236, comma 5.

Publications

Conference papers

1. **M.A. Pirozzi**, E. Andreozzi, M. Magliulo, P. Gargiulo, M. Cesarelli, B. Alfano, *Automated Design of Efficient Supports in FDM 3D Printing of Anatomical Phantoms*. In: Henriques J., Neves N., de Carvalho P. (eds) XV Mediterranean Conference on Medical and Biological Engineering and Computing – MEDICON 2019. MEDICON 2019. IFMBE Proceedings, vol 76. Springer, Cham. https://doi.org/10.1007/978-3-030-31635-8_35
2. E. Andreozzi, **M.A. Pirozzi**, A. Sarno, D. Esposito, M. Cesarelli, P. Bifulco, *A Comparison of Denoising Algorithms for Effective Edge Detection in X-Ray Fluoroscopy*. In: Henriques J., Neves N., de Carvalho P. (eds) XV Mediterranean Conference on Medical and Biological Engineering and Computing – MEDICON 2019. MEDICON 2019. IFMBE Proceedings, vol 76. Springer, Cham. https://doi.org/10.1007/978-3-030-31635-8_49
3. E. Andreozzi, **M.A. Pirozzi**, A. Fratini, G. Cesarelli and P. Bifulco, *Quantitative performance comparison of derivative operators for intervertebral kinematics analysis*, 2020 IEEE International Symposium on Medical Measurements and Applications (MeMeA), Bari, Italy, 2020, pp. 1-6, doi: 10.1109/MeMeA49120.2020.9137322.
4. E. Andreozzi, **M.A. Pirozzi**, A. Fratini, G. Cesarelli, M. Cesarelli and P. Bifulco, *A Novel Image Quality Assessment Index for EdgeAware Noise Reduction in Low-Dose Fluoroscopy:Preliminary Results*, 2020 International Conference on e-Health and Bioengineering (EHB), Iasi, Romania, 2020, pp. 1-5, doi: 10.1109/EHB50910.2020.9280107.
5. **M.A. Pirozzi**, E. Andreozzi, M. Magliulo, P. Gargiulo, M. Cesarelli, B. Alfano, *3D-printed anatomical phantoms for medical imaging applications*, Proceedings of the 18th Nordic-Baltic Conference on Biomedical Engineering (NBC), Reykjavik, Iceland, 2020 (Article in press).

Publications

Journal papers

1. A. Canna, A. Prinster, M. Fratello, L. Puglia, M. Magliulo, E. Cantone, **M. A. Pirozzi**, F. Di Salle, F. Esposito, *"A low-cost open-architecture taste delivery system for gustatory fMRI and BCI experiments"*, Journal of Neuroscience Methods, Volume 311, 2019, Pages 1-12, ISSN 0165-0270, https://doi.org/10.1016/j.jneumeth.2018.10.003.
2. **M.A. Pirozzi**, M. Tranfa, M. Tortora, R. Lanzillo, V. Brescia Morra, A. Brunetti, B. Alfano, M. Quarantelli, *"A polynomial regression-based approach to estimate relaxation rate maps suitable for multiparametric segmentation of clinical brain MRI studies in multiple sclerosis."*. [Under Review - Medical Image Analysis journal].
3. C. Russo*, **M.A. Pirozzi***, B. Alfano, F. Mazio, D. Cascone, D. Cicala, M. De Liso, A. Nastro, E.M. Covelli, G. Cinalli, M. Quarantelli, *"Fully automated measurement of intracranial CSF volume by segmentation of clinical MRI studies in pediatric patients with severe anatomical alterations."*. [In preparation]
4. **M.A. Pirozzi**, M. Magliulo, M. Cesarelli, M. Quarantelli, B. Alfano (partial list), *"3D-printed multicompartmental anthropomorphic brain phantom for morpho-functional imaging applications"*. [In preparation]
5. **M.A. Pirozzi**, M. Quarantelli, B. Alfano (partial list), *"An innovative approach for automatic brain segmentation based on MRI relaxation parameter maps"*. [In preparation]

* These authors share first autorship

Book Chapter

I have been involved in writing *Section A - 3D printing (3DP) in Healthcare, General Part* of a presurgical planning 3D printing handbook, which will be published by **Elsevier**, presumably in early 2022.

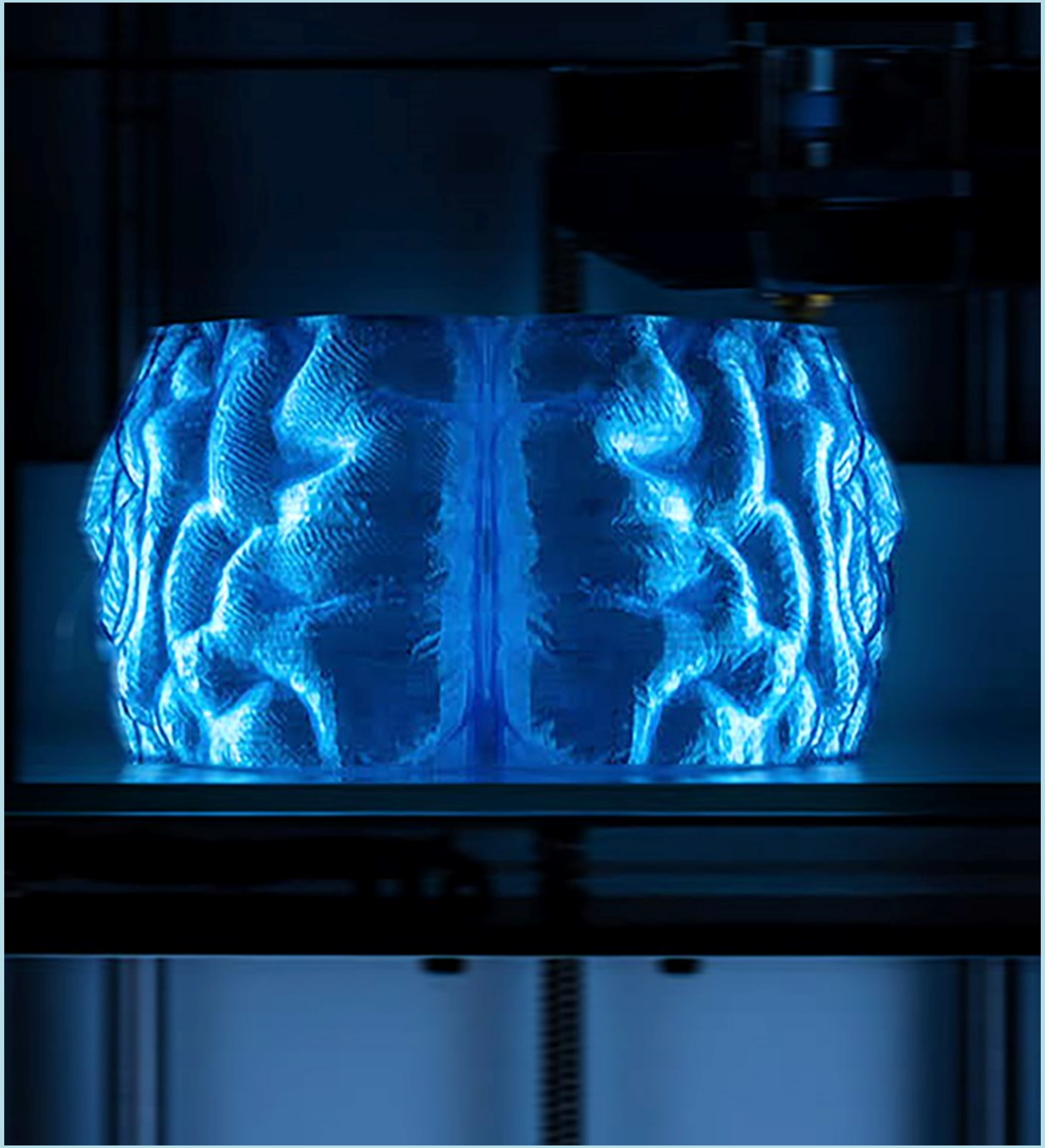
Main Collaborations

In Italy

- Department of Advanced Biomedical Sciences, University of Naples “Federico II”
- Department of Neurosciences and Reproductive and Odontostomatological Sciences, University of Naples “Federico II”

Abroad

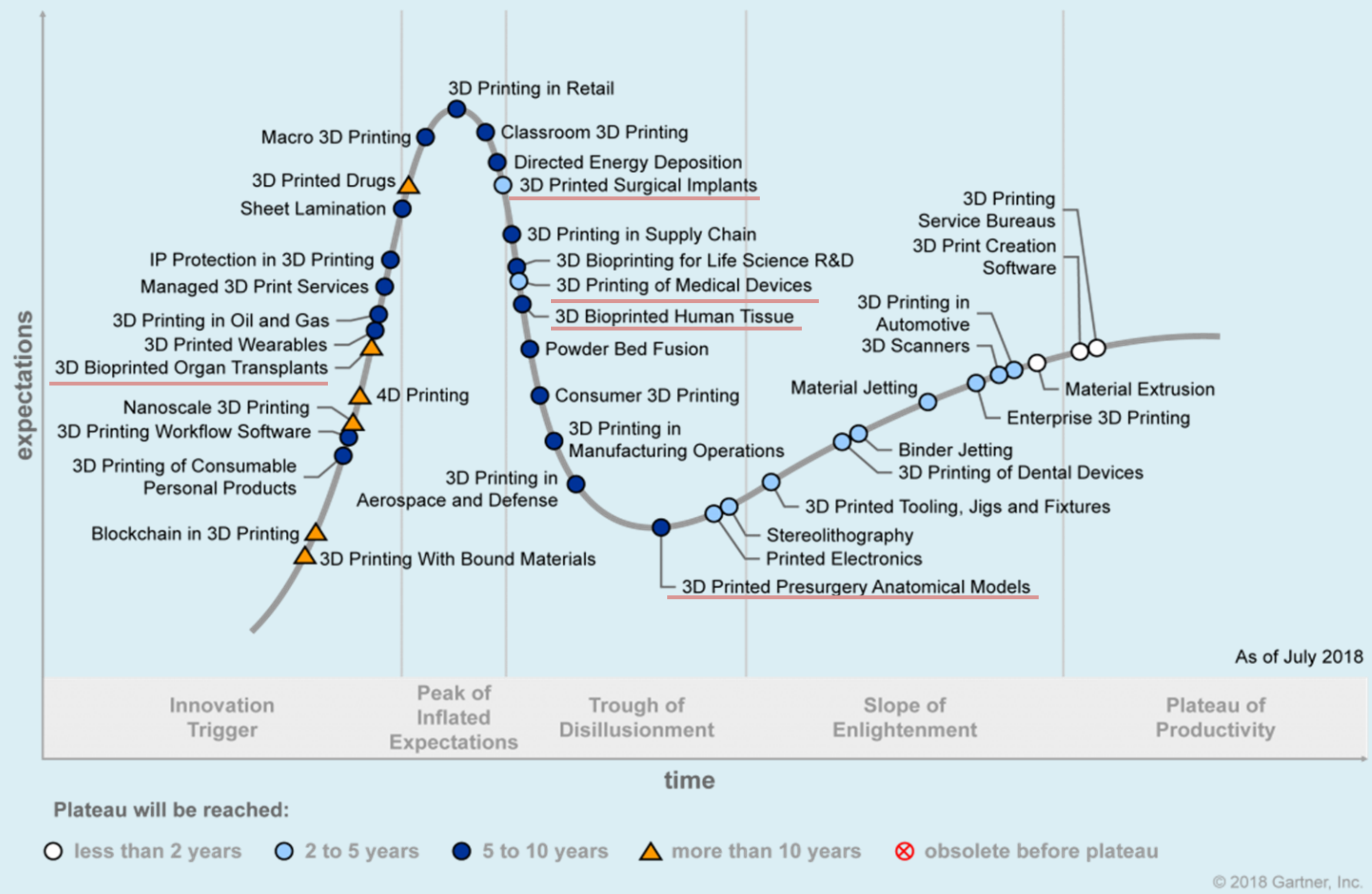
Reykjavik University, School of Technology, Department of Engineering, Medical Technology Center



3D Printing
in
Biomedical Applications

Research context

3D Printing (3DP) Hype Cycle



Increasing use of **Additive Manufacturing (AM)** in biomedical field for:

- pre-surgical planning
- surgical implants
- joint replacements
- prostheses
- medical education and training

Prediction

By 2023, 25% of medical devices in developed markets will make use of 3D printing.

Research context

Why 3DP in Biomedical Applications?

AM materializes objects in an additive way (i.e., *layer-by-layer*), making the creation of products no longer constrained by the complexity of the design.

VERSATILITY

Capacity of manufacturing different anatomical models

CUSTOMIZATION

Customized products and personalized models

IMMEDIACY

3D models in the hands of physician and patients

EASE OF ACCESS

Large number of 3D printers entering the industry

Anthropomorphic Brain Phantoms

Research context

Anatomical Phantoms

Anthropomorphic phantoms play a key role in medical imaging research as they provide controlled experimental environments for the improvement of medical imaging techniques.

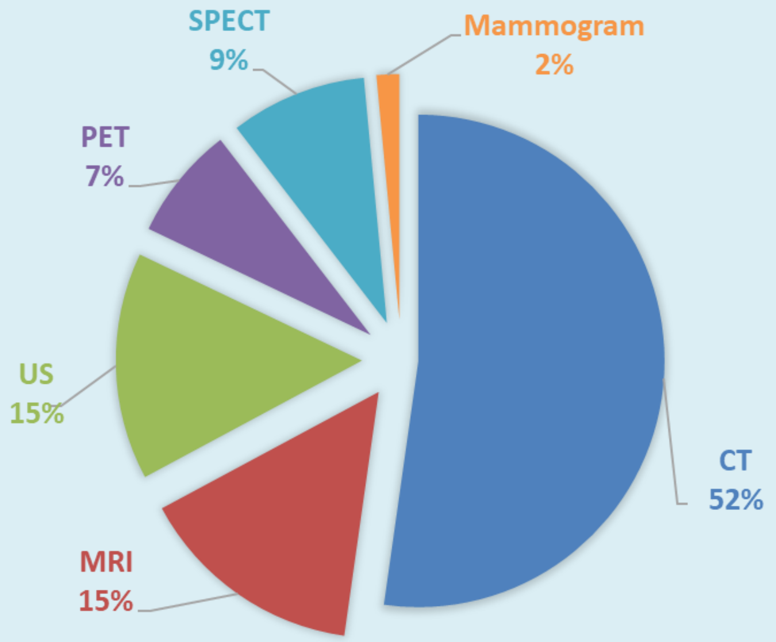
Advanced test objects to simulate real patients in morpho-functional imaging applications.

Research context

Anatomical Phantoms

3D-printed anatomical phantoms derived from medical images are only recently proposed as the next revolution for quantitative and technical evaluations on radiological imaging devices.

Number of research articles that used these imaging modalities to scan the 3D-printed phantoms (starting with CT clockwise).

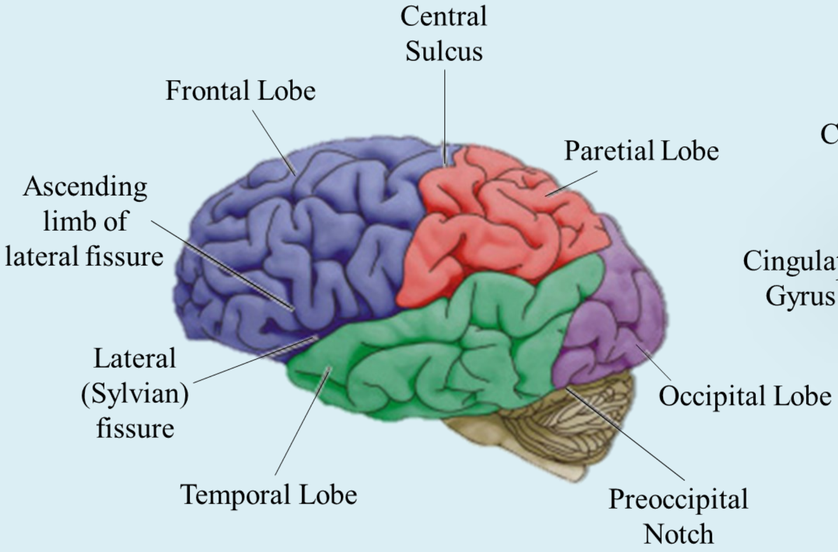


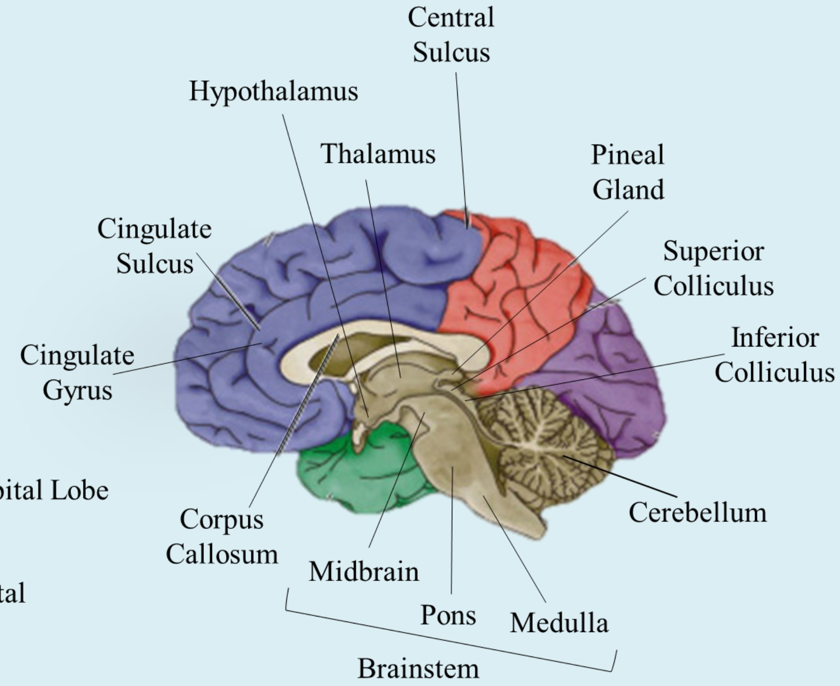
Filippou, V., Tsoumpas, C.: Recent advances on the development of phantoms using 3D printing for imaging with CT, MRI, PET, SPECT, and ultrasound. Med. Phys. 45, e740-e760 (2018).

Research context

Brain Anatomy

The human brain is a functionally and topologically complex organ, richly innervated, with deep sulci and convolutions on its surfaces (medial and lateral), and fluid that fills the ventricles (cerebrospinal fluid – CSF).



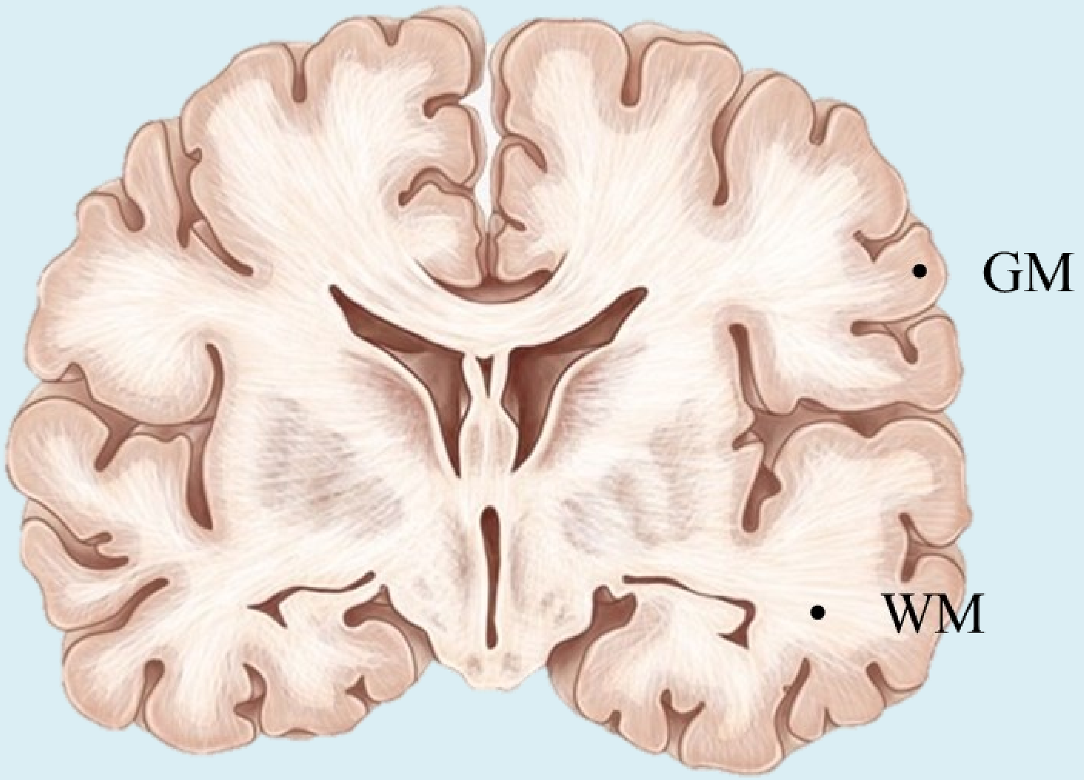


Research context

Brain Anatomy

The main constituents are Grey Matter (GM), mainly located on the cortex, and White Matter (WM), found buried in the inner layer of the cortex.

Frontal section of cerebrum

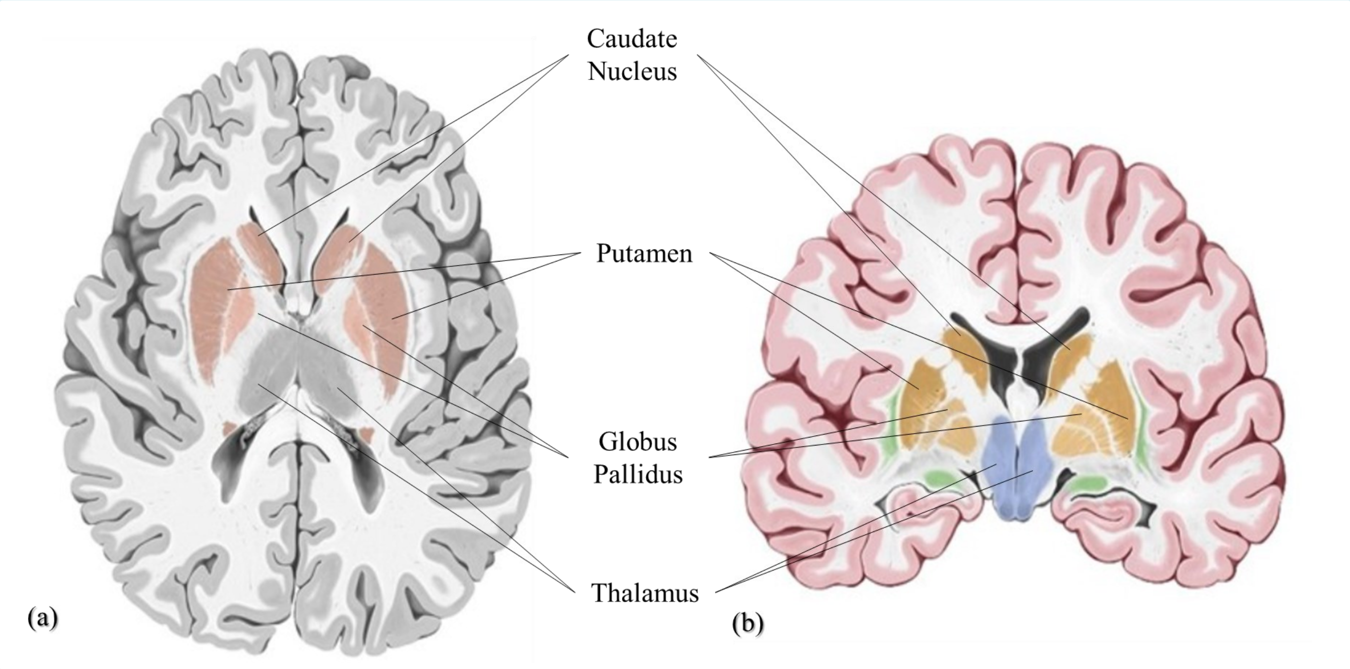


Research context

Brain Anatomy

The main constituents are Grey Matter (GM), mainly located on the cortex, and White Matter (WM), found buried in the inner layer of the cortex.

Aggregates of GM, surrounded by deep cerebellar WM (arbor vitae), are also distributed in the depths of the cerebrum (hypothalamus, thalamus, subthalamus, basal ganglia).



Research context

Applications of Brain Phantoms

Phantoms are designed to reproduce morphological details of brain tissues, providing at the same time empty volumes to be filled with solutions that mimic their physiological properties.

Phantom-based imaging studies (CT, MRI, PET, SPECT and hybrid modalities PET-SPECT/CT, PET-MRI) are carried out to:

- reduce quantitative variability due to differences in the acquisition setting
- verify the calibration of scanner
- the capability of each scanner to support specific brain imaging modalities

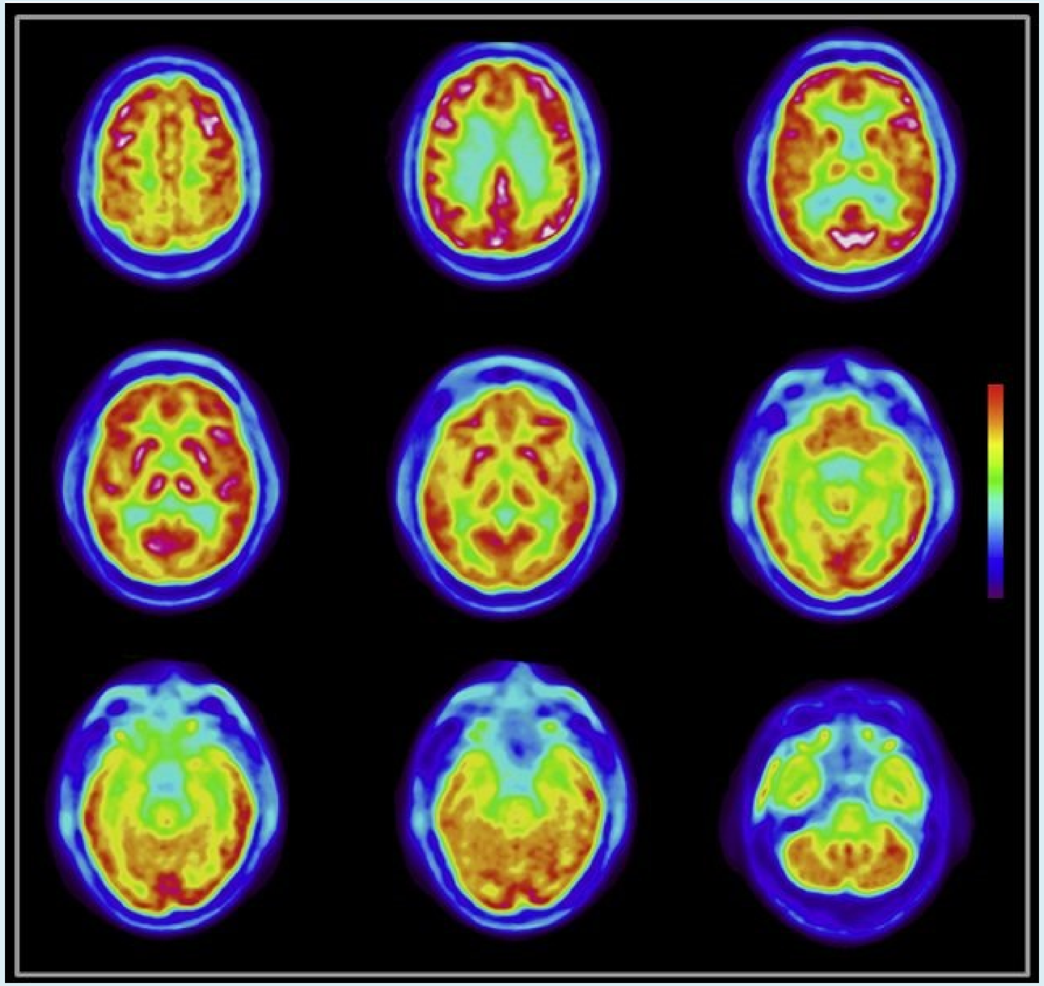
Research context

Applications of Brain Phantoms

Anatomical brain phantoms are mainly designed to carry out the accuracy measurements of the Emission Computed Tomography (ECT) systems in nuclear medicine studies.

Inaccuracies in Nuclear Medicine Studies due to:

- Registration error
- Limited spatial resolution
- Partial volume effect
- Noise on images

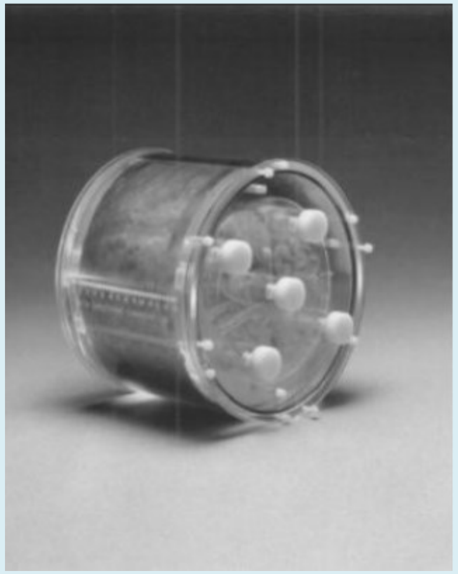
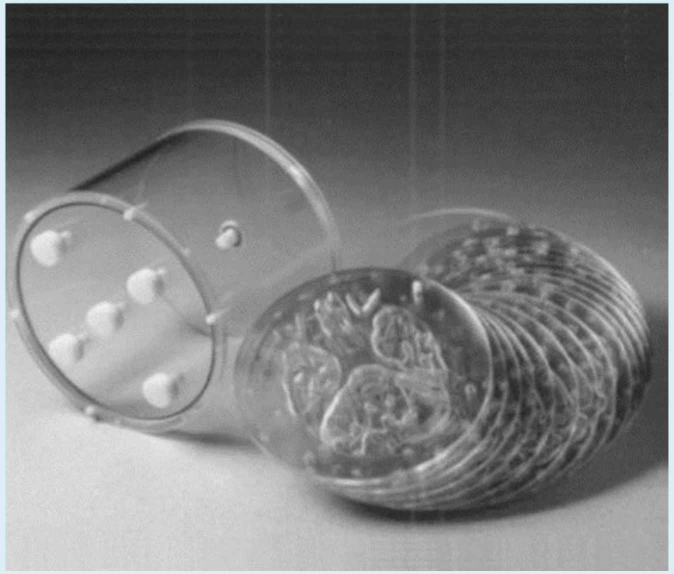
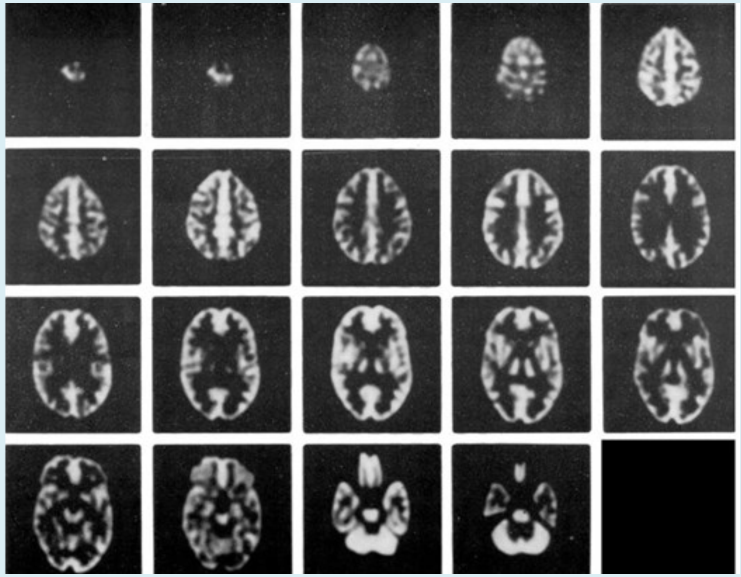


Normal distribution of FDG uptake in the brain. Axial images of a healthy volunteer*. Figure license: Michael Schöll et al., "Fluorodeoxyglucose PET in Neurology and Psychiatry", PET Clinics*

Research context

Commercial Brain Phantoms

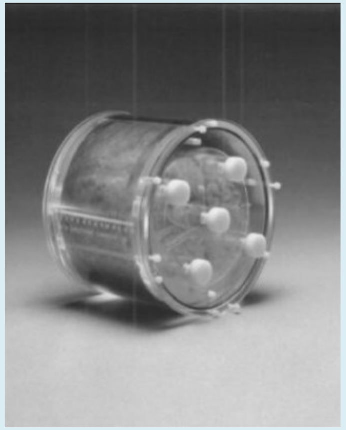
3D Hoffman Brain Phantom for Nuclear Medicine

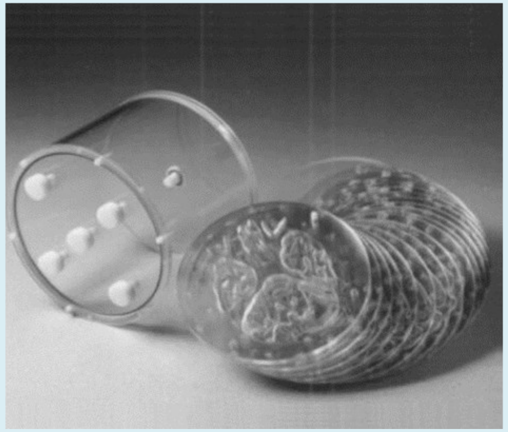




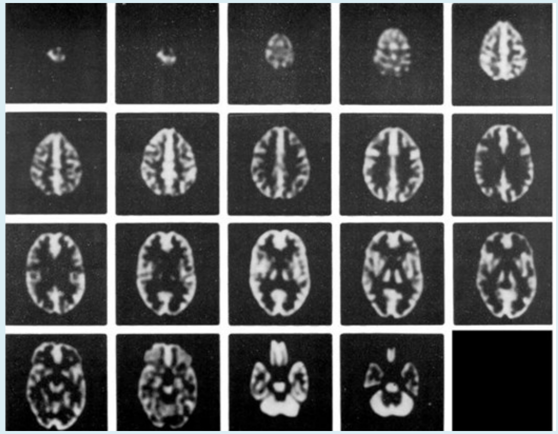
Research context

Commercial Brain Phantoms

3D Hoffman Brain Phantom for Nuclear Medicine





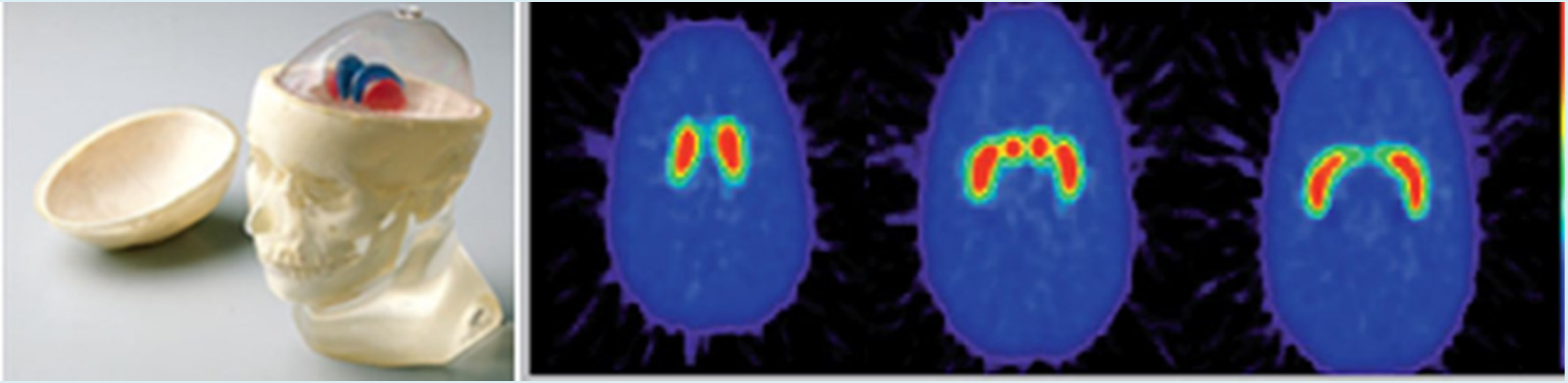


This phantom can reproduce a GM to WM tracer concentration ratio of 4 to 1, which is considered representative of the physiological range.

Research context

Commercial Brain Phantoms

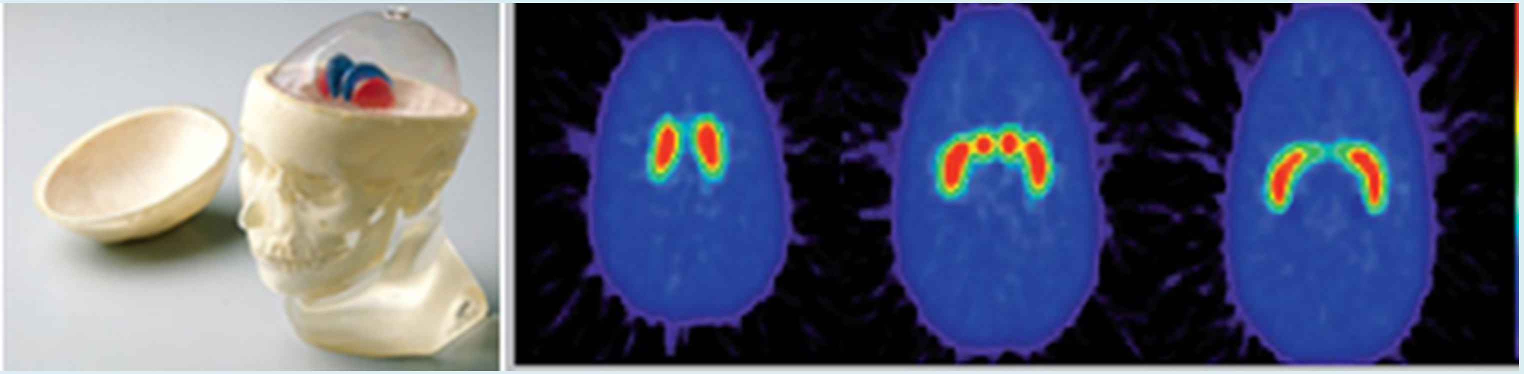
RSD Alderson Striatal Phantom for SPECT/PET



Research context

Commercial Brain Phantoms

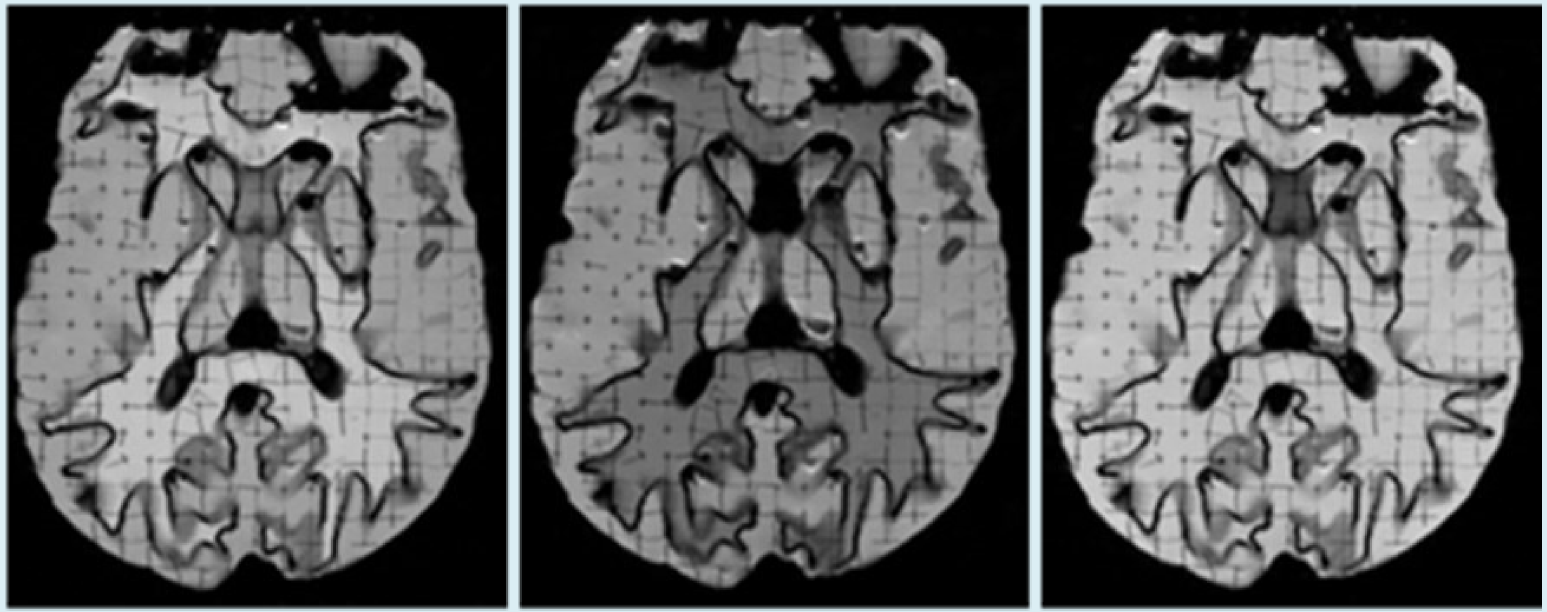
RSD Alderson Striatal Phantom for SPECT/PET



This phantom simulates different caudate to putamen ratios, as well as different striatal to background ratios.

Research context

STEPBrain Phantom

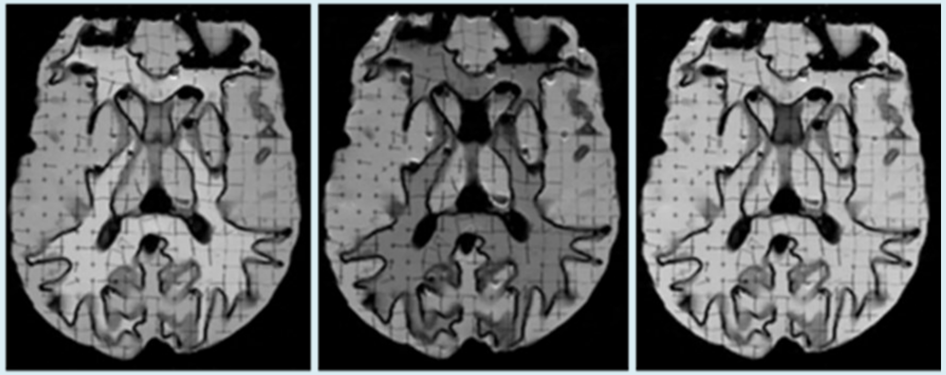


STEPBRAIN. US Patent number: 2006-0166353-A1 (July 27, 2006).

Research context

STEPBrain Phantom

Multi-compartmental and multi-analytical anatomical brain phantom made by stereolithography, the first 3D printing technology.

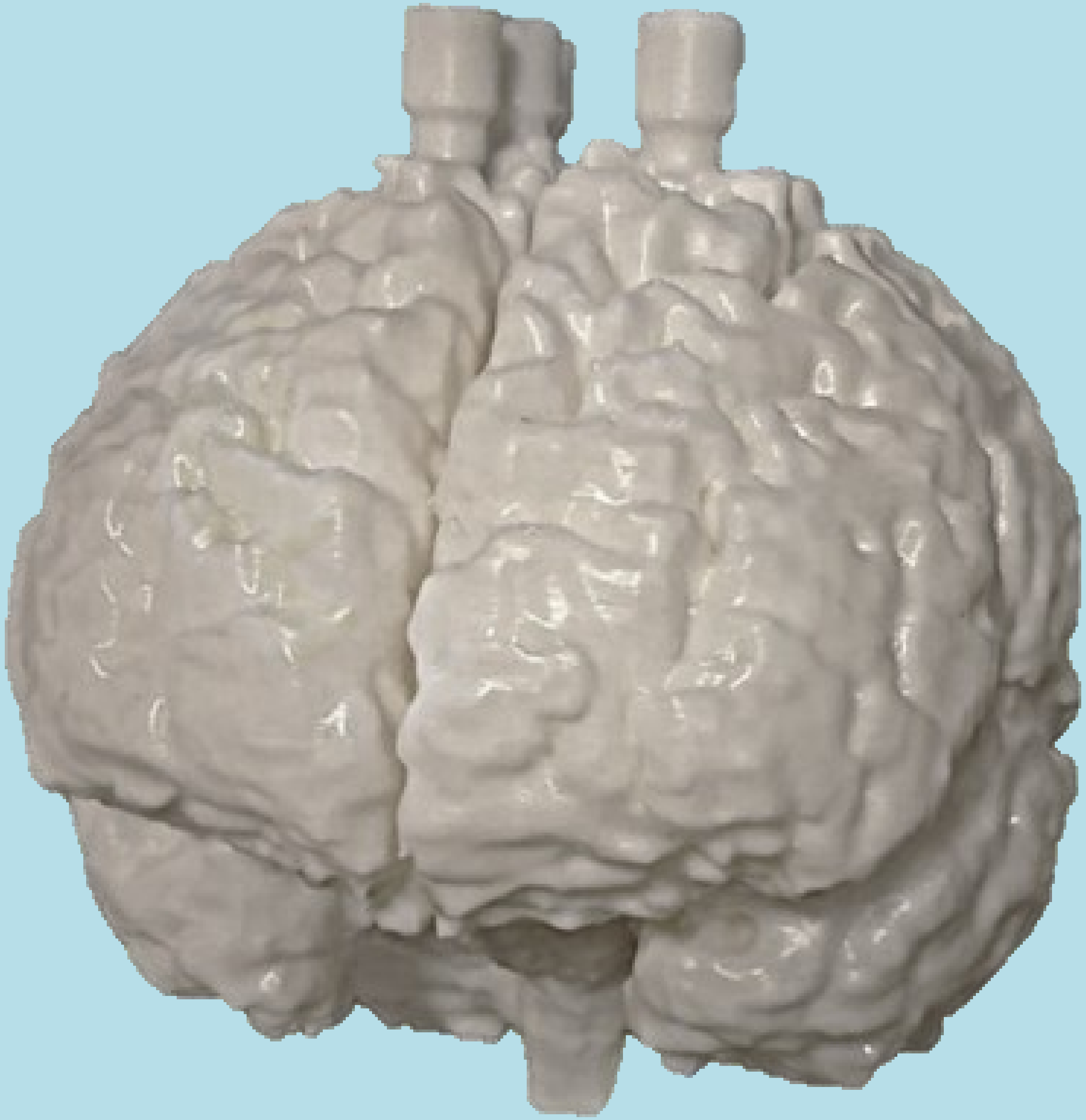


This phantom is composed of two separate compartments for GM and WM, which can be filled with solutions with different concentrations of:

- radioactive isotopes for PET/SPECT;
- para-/ferromagnetic metals for MRI;
- iodine for CT.

The normal 4 to 1 ratio of GM to WM in FDG concentration can be simulated.

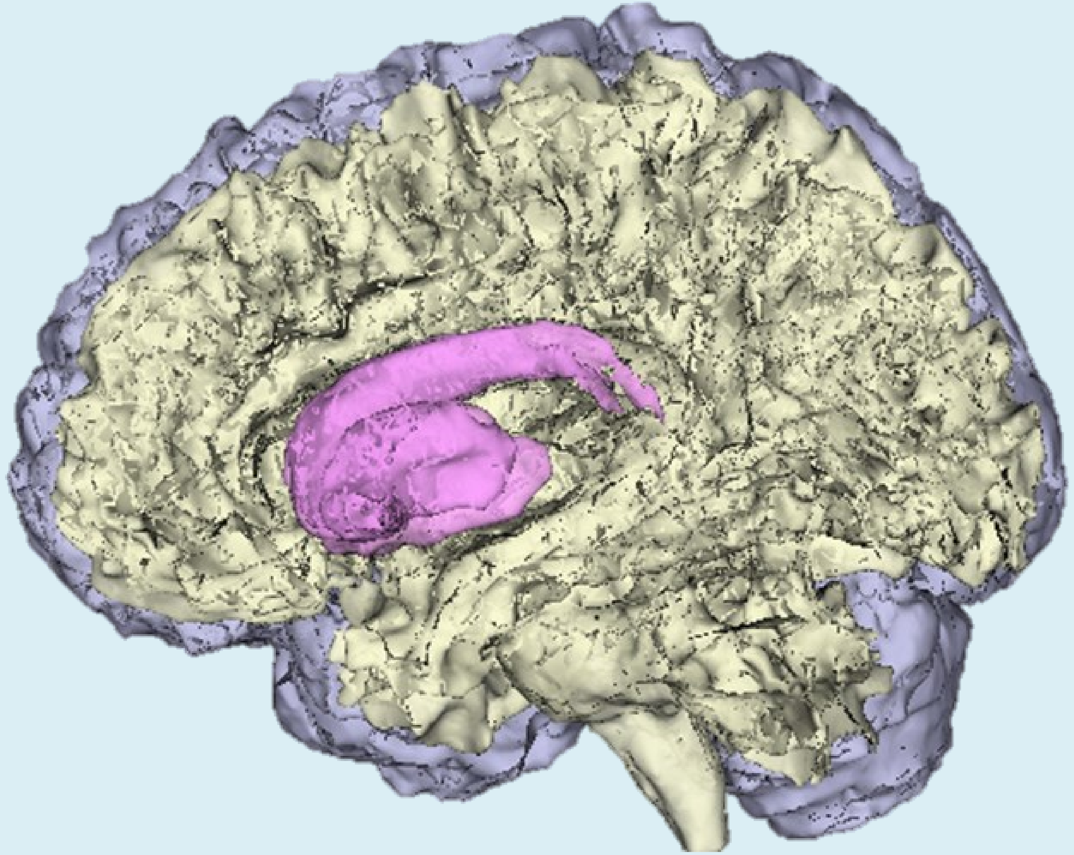
STEPBRAIN. US Patent number: 2006-0166353-A1 (July 27, 2006).



The New Anthropomorphic Brain Phantom

Idea

Technical Specifications

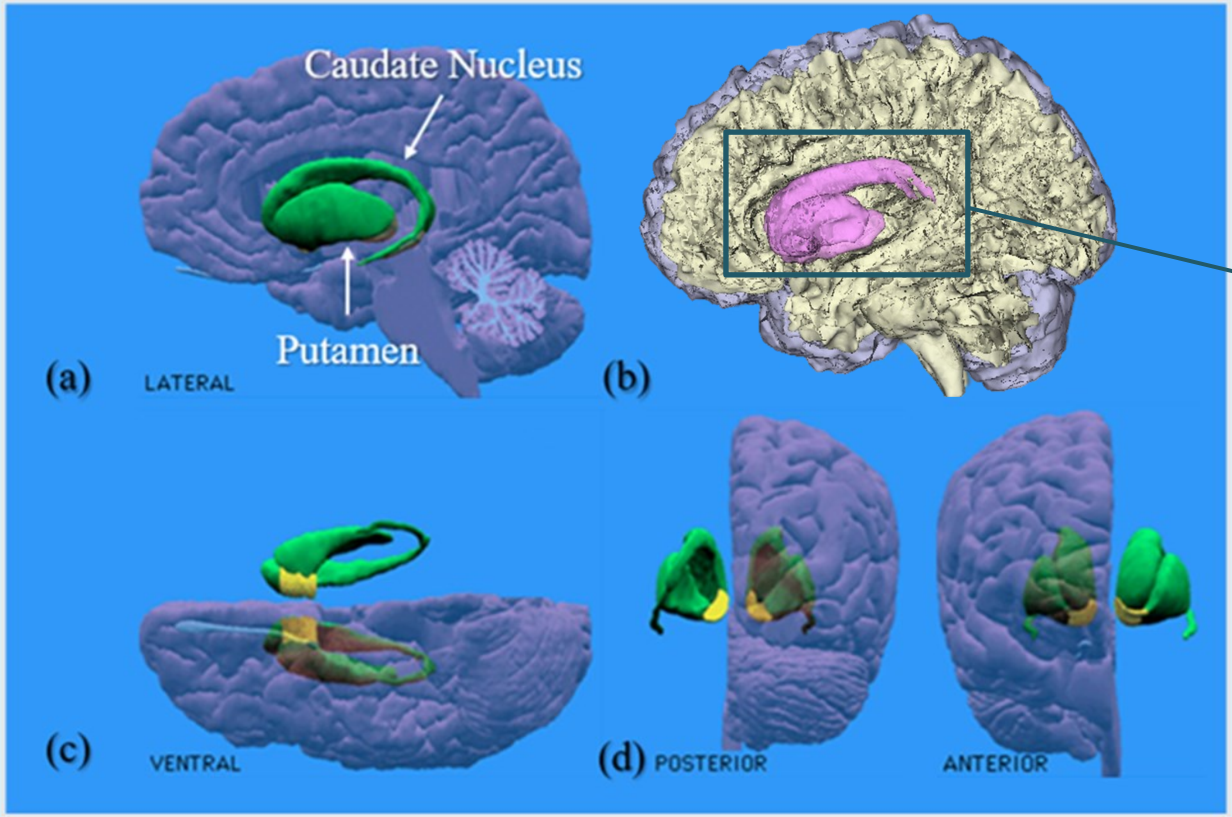


Three separate brain compartments:

- Gray Matter (GM)
- White Matter (WM)
- Striatum

Idea

Technical Specifications



Three separate brain compartments:

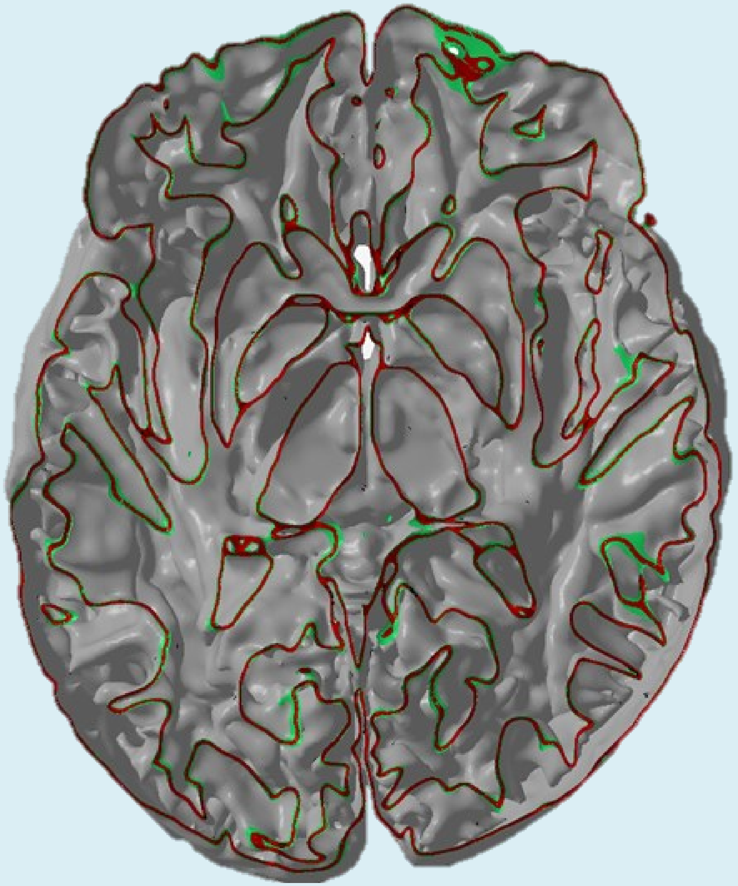
- Gray Matter (GM)
- White Matter (WM)
- Striatum

Caudate Nucleus + Putamen

It shows a high uptake in nuclear medicine studies.

Idea

Technical Specifications



Three separate brain compartments:

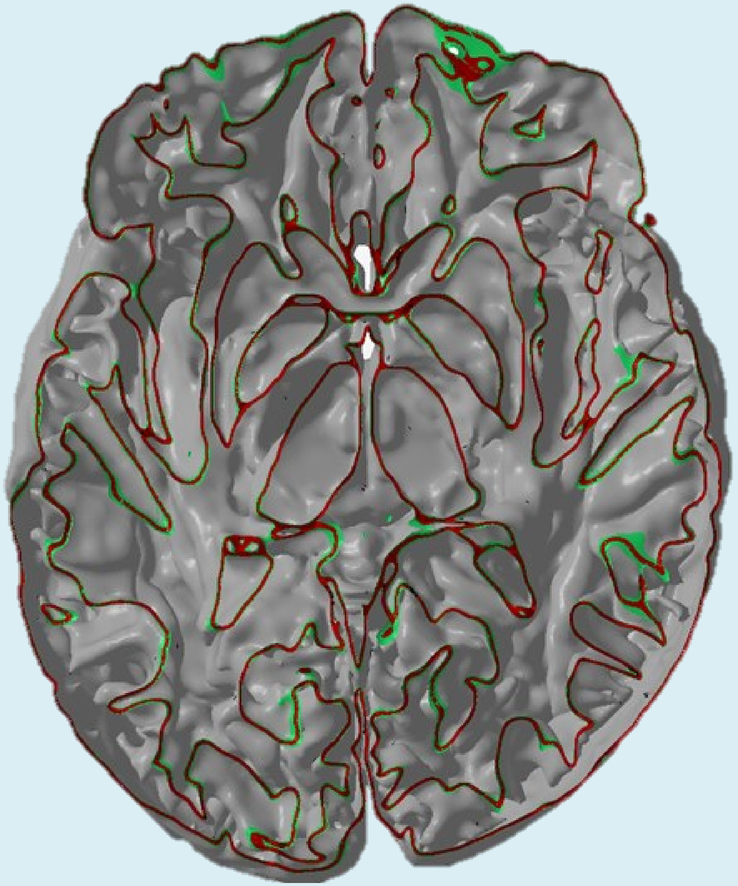
- Gray Matter (GM)
- White Matter (WM)
- Striatum

Wall thickness

The walls of the three (hollow) compartments of the new brain phantom should ideally have a sub-millimetre thickness, preferably in the range between 0.4 – 1 mm.

Idea

Technical Specifications



Three separate brain compartments:

- Gray Matter (GM)
- White Matter (WM)
- Striatum

Waterproofness

To avoid any leakage to the outside, or between the compartments, for a good simulation by means of different solutions for different brain imaging modalities.

Methods

Workflow

1 **MEDICAL IMAGING**

High-resolution acquisition of brain images (MRI)

2 **IMAGE POST-PROCESSING**

3D model from segmented medical images

3 **STL EXTRACTION**

Interface format suitable for 3D Printing

4 **MESH REFINEMENT**

Manifoldness check and mesh correction

5 **SLICING**

L7 ⋮ L1

STL model is sliced by means of slicing software

6 **3D PRINTING**

Ready to print?!

Methods

Workflow

No standardized procedure to extract 3D-printable phantoms from medical images.

1

MEDICAL IMAGING

High-resolution acquisition of brain images (MRI)

2

IMAGE POST-PROCESSING

3D model from segmented medical images

3

STL EXTRACTION

Interface format suitable for 3D Printing

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MESH REFINEMENT

Manifoldness check and mesh correction

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SLICING

STL model is sliced by means of slicing software

6

3D PRINTING

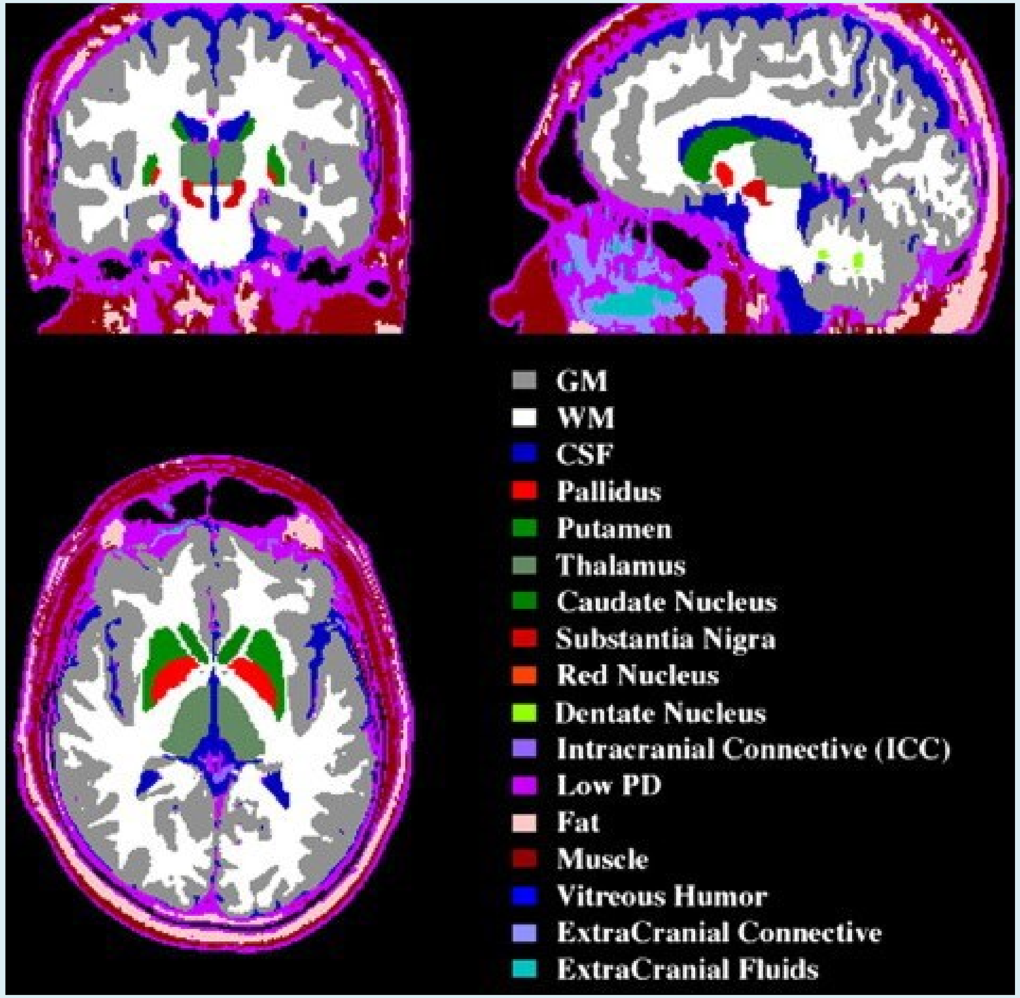
Ready to print?!

Methods

2 Digital Brain Phantom - *Phantomag*

- Derived from Conventional Spin-Echo (CSE) acquisition on a 1.5T scanner of a 38 years old male normal volunteer.
- MRI data consists of 150 axial slices, with a near-isotropic voxel of 0.9375×0.9375×1 mm^3 (interpolated for 3D modelling to bring it to a voxel resolution of 0.5×0.5×0.5 mm^3).
- Composed of 17 compartments of segmented healthy brain tissue, plus an optional eighteenth compartment that simulates multiple sclerosis (abnormal white matter) lesions.
- A "gold standard" against which the automatic segmentation of software can be compared.

B. Alfano et al., "An MRI digital brain phantom for validation of segmentation methods", Medical image analysis, vol. 15, no. 3, pp. 329-339, 2011



Methods

2 Design of Phantom Compartments

Brain segmentation must necessarily to be refined for 3DP to meet the design specifications and printability criteria.

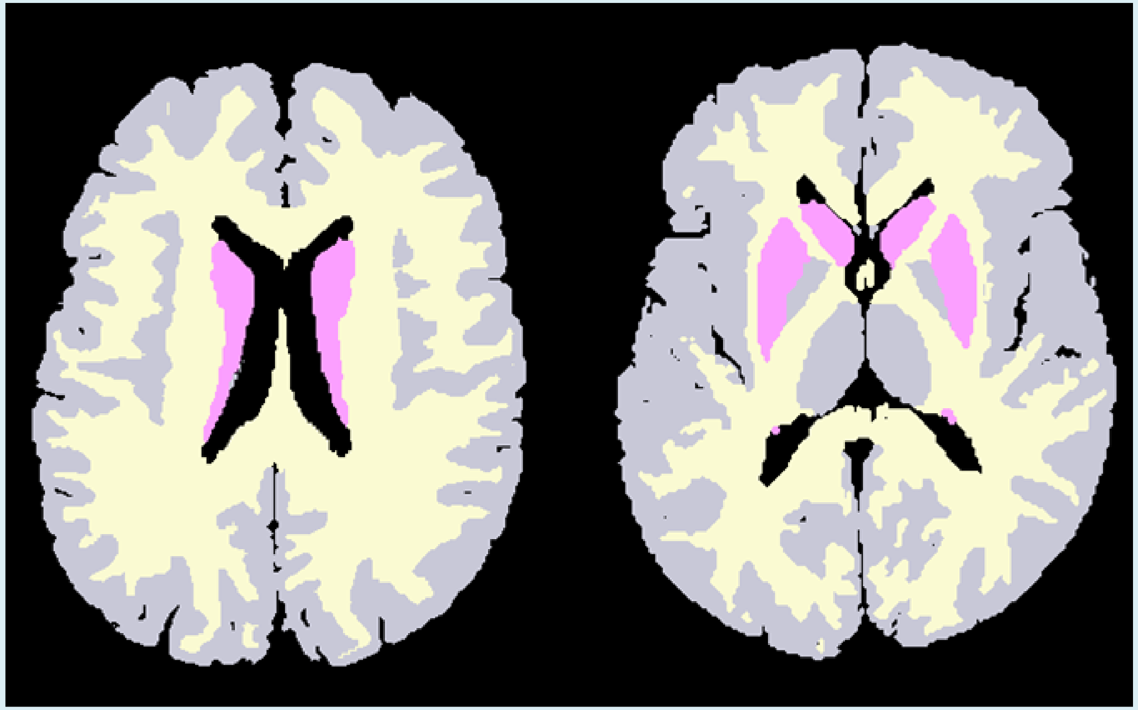
Methods

2 Design of Phantom Compartments

Brain segmentation must necessarily to be refined for 3DP to meet the design specifications and printability criteria.

Automatic pipeline to obtain three separate brain compartments for GM, WM e Striatum:

1. association of the other tissues to the three of interest



Methods

2 Design of Phantom Compartments

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Automatic pipeline to obtain three separate brain compartments for GM, WM e Striatum:

1. association of the other tissues to the three of interest
2. elimination of "voxel islands" three-dimensionally disconnected from the main compartment

On the *Phantomag* phantom were identified:

- 47 clusters for the GM compartment
- 19 clusters were identified for the WM compartment
- 4 clusters, corresponding to the two caudate nuclei and two putamina, for the striatum

Methods

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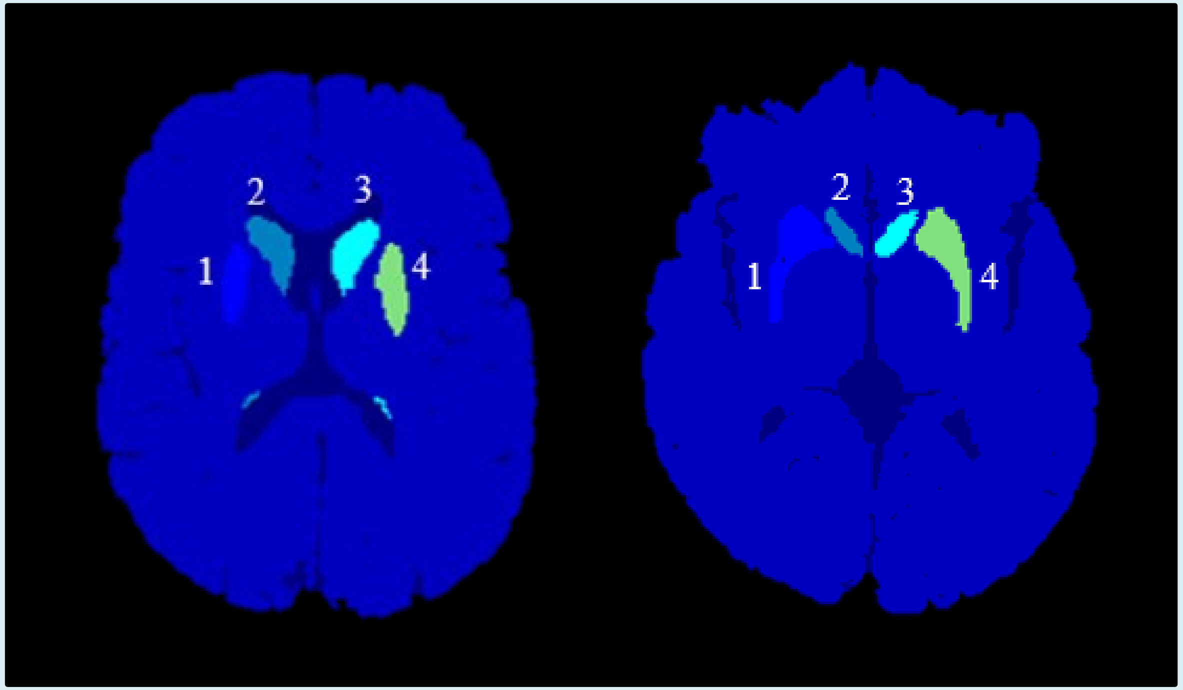

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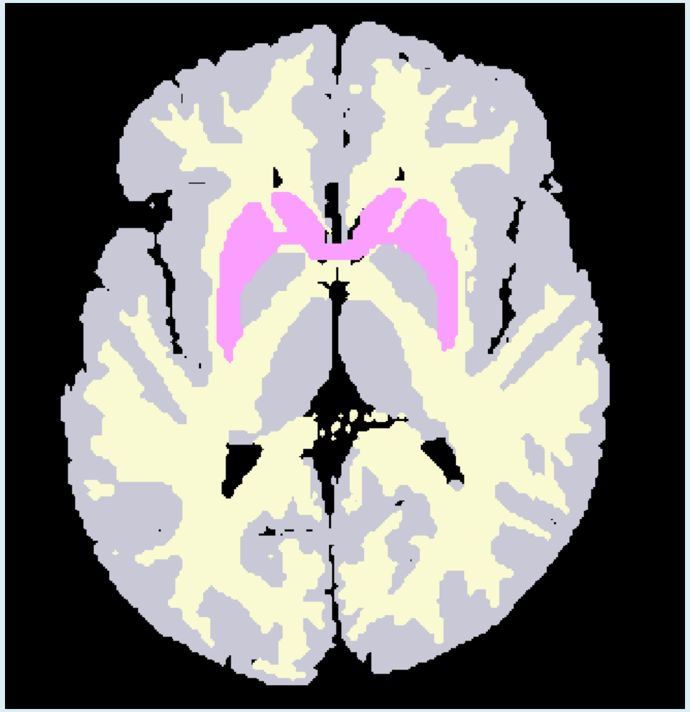
3. connection of the 4 parts of the striatum



Methods

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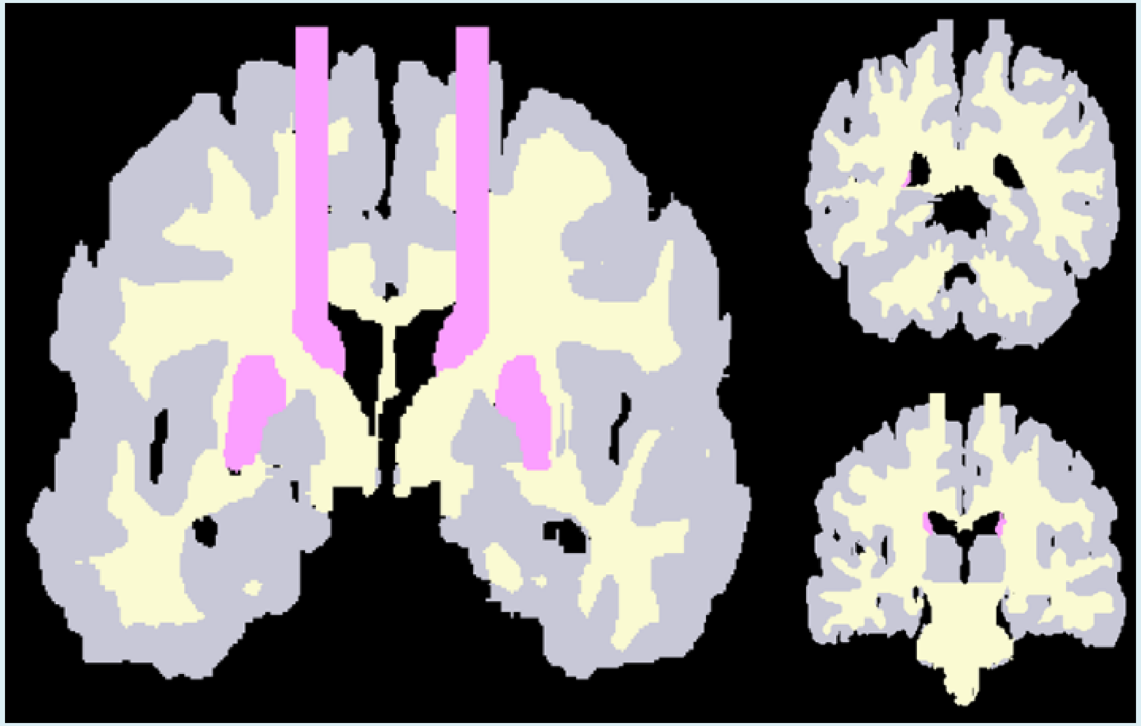
2. elimination of "voxel islands" three-dimensionally disconnected from the main compartment
3. connection of the 4 parts of the striatum
4. insertion of the tubes of access to different compartments for filling



Methods

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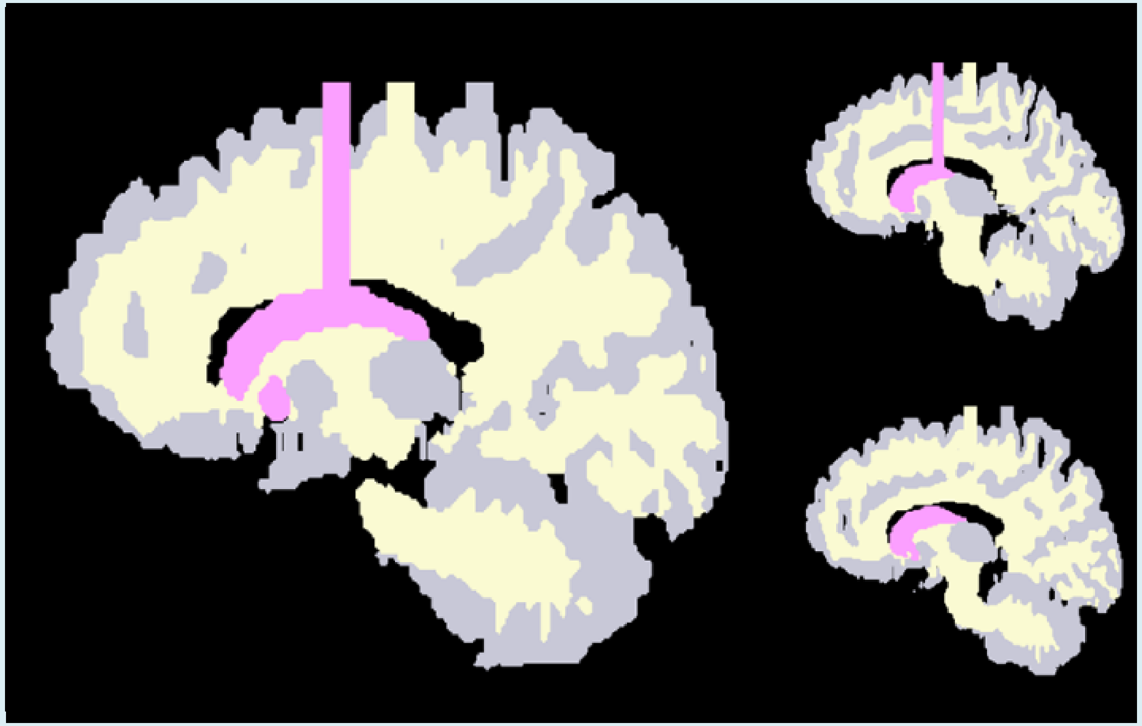
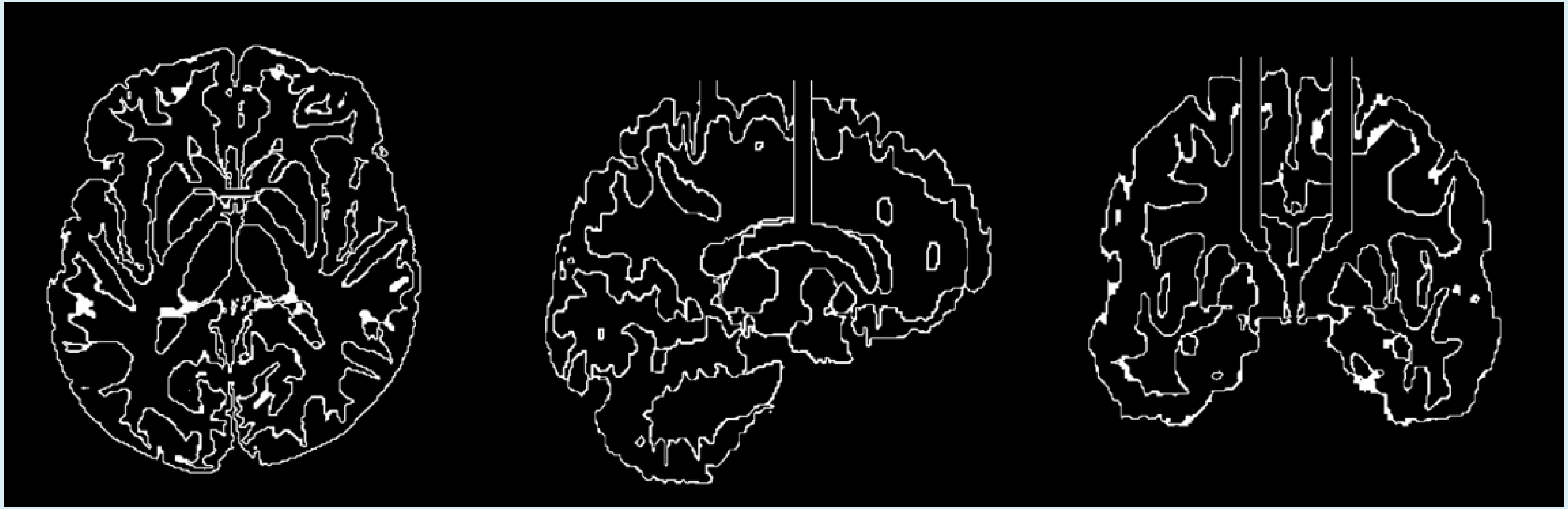
2. elimination of "voxel islands" three-dimensionally disconnected from the main compartment
3. connection of the 4 parts of the striatum
4. insertion of the tubes of access to different compartments for filling



Methods

2 Extraction of Voxelized Surfaces

The surfaces at the interface between the various compartments can be defined in terms of voxels (voxelized surfaces) to realize a minimum wall thickness of compartments equal to 0.5 mm.



Methods

Workflow

1 **MEDICAL IMAGING**

High-resolution acquisition of brain images (MRI)

2 **IMAGE POST-PROCESSING**

3D model from segmented medical images

3 **STL EXTRACTION**

Interface format suitable for 3D Printing

4 **MESH REFINEMENT**

Manifoldness check and mesh correction

5 **SLICING**

STL model is sliced by means of slicing software

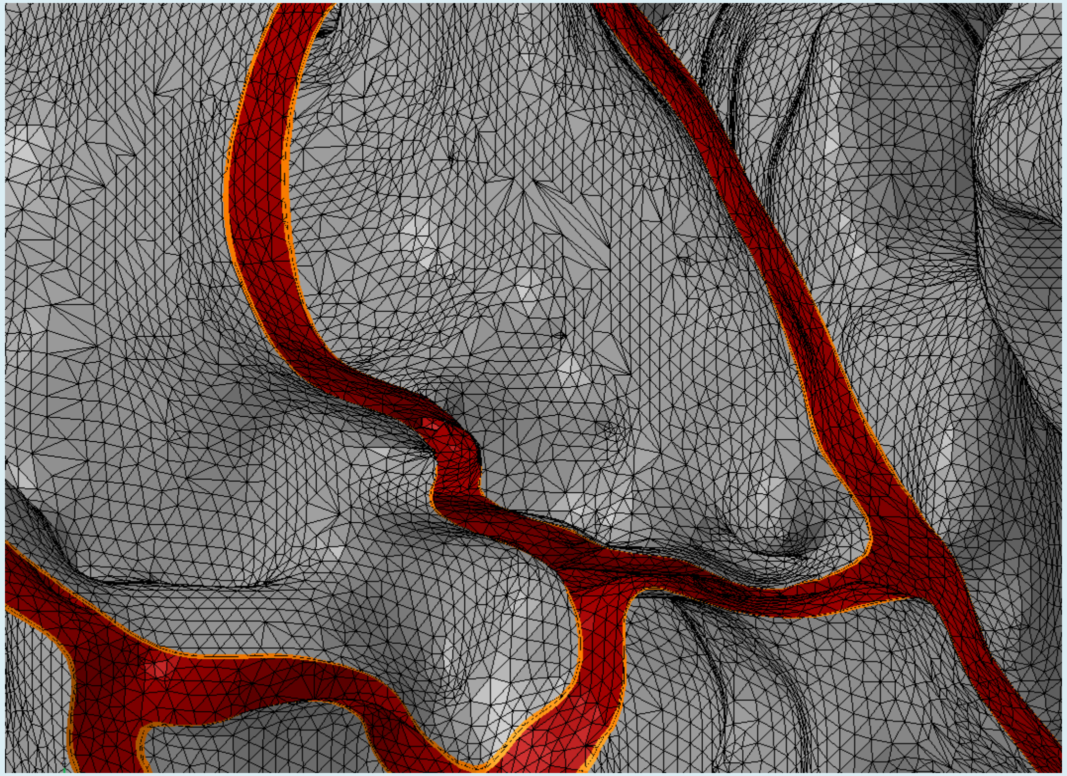
6 **3D PRINTING**

Ready to print?!

Methods

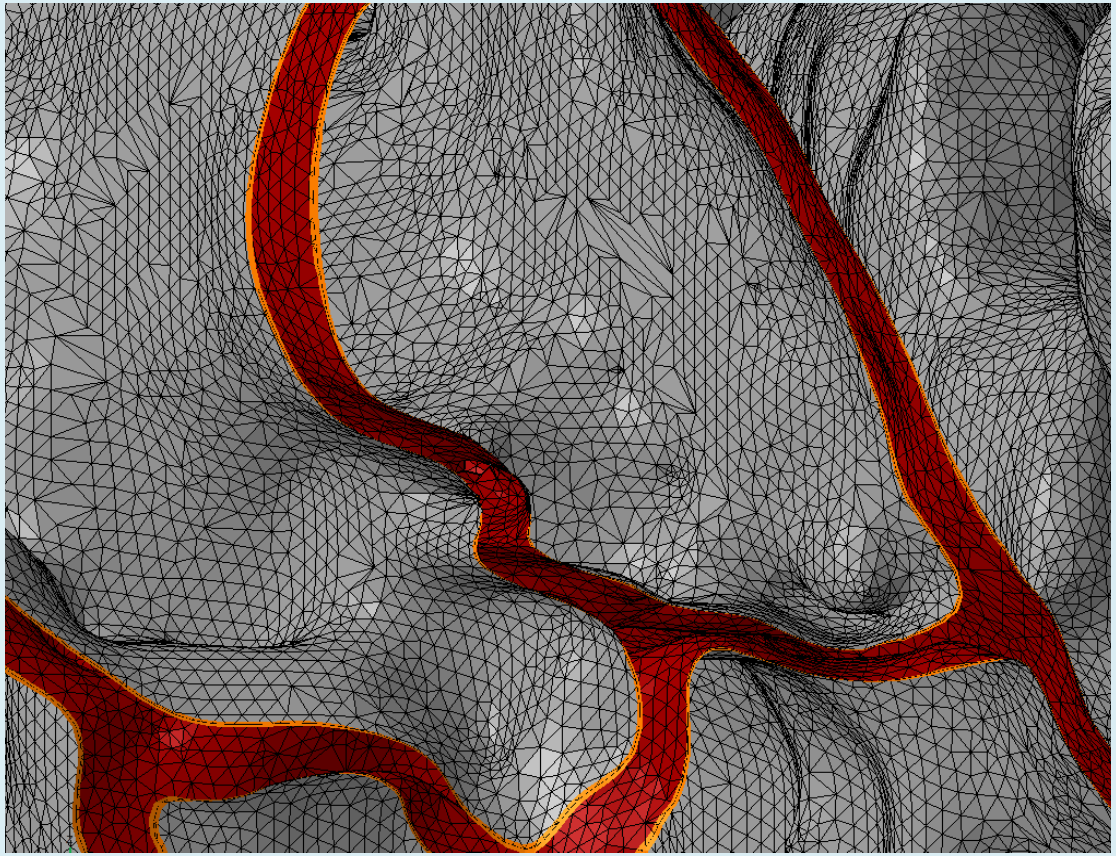
3 Extraction of Polygonal Mesh-based Phantom

The standard file format for defining the surfaces of a 3D model is the Standard Tessellation Language (STL).



Methods

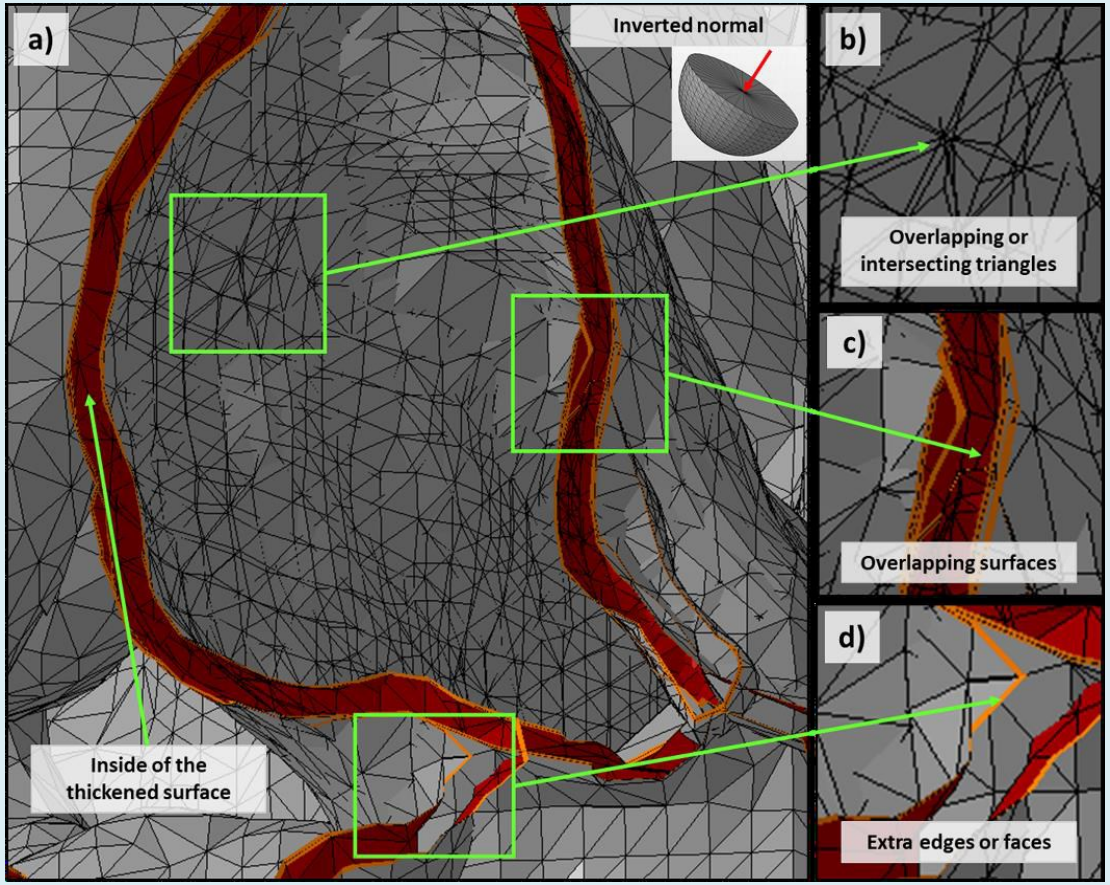
3 Extraction of Polygonal Mesh-based Phantom



The polygonal mesh must be topologically manifold:

Methods

3 Extraction of Polygonal Mesh-based Phantom



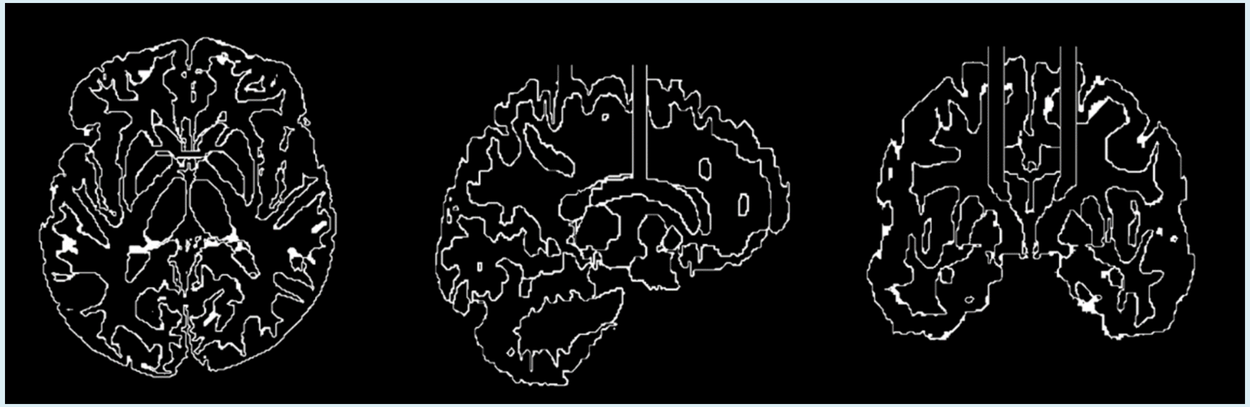
The polygonal mesh must be topologically manifold:

- No inverted normal
- No overlapping or intersecting triangles
- No extra edges or faces hidden within the 3D structure
- No bad-edges
- No noise-shells
- Water-tight mesh

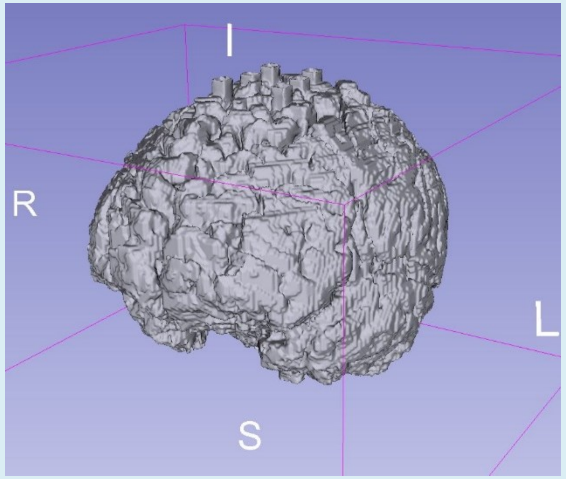
Methods

3 Extraction of Polygonal Mesh-based Phantom

The polygonal mesh of the phantom can be done using a medical image-to-STL conversion software, 3D Slicer, employing a high-resolution 3D surface construction algorithm, called Marching Cubes.



STL EXTRACTION



- A. Fedorov et al., "3D Slicer as an image computing platform for the Quantitative Imaging Network," Magnetic Resonance Imaging, vol. 30, no. 9, pp. 1323-1341, 2012/11/01

- W. E. Lorensen and H. E. Cline, "Marching cubes: A high resolution 3D surface construction algorithm," presented at the Proceedings of the 14th annual conference on Computer graphics and interactive techniques, 1987. Available: https://doi.org/10.1145/37401.37422

Methods

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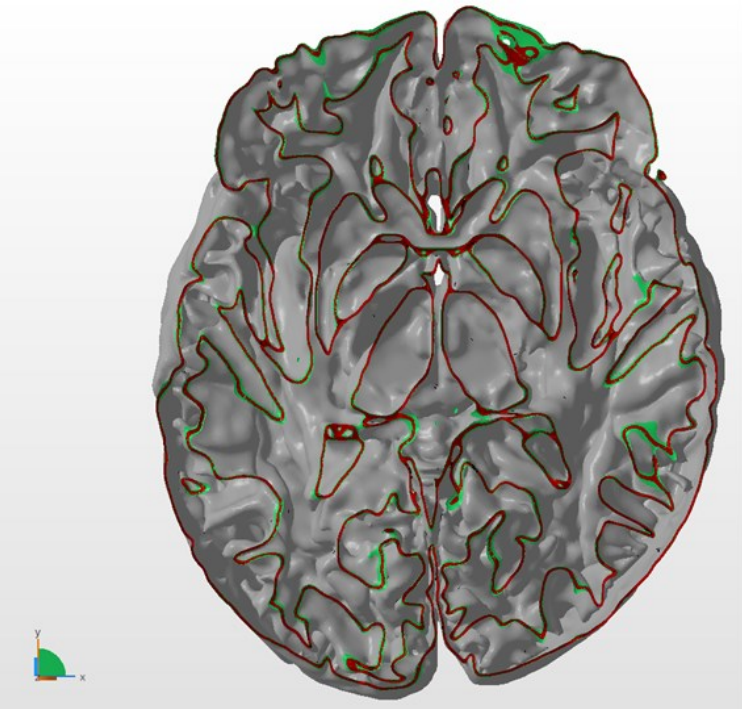
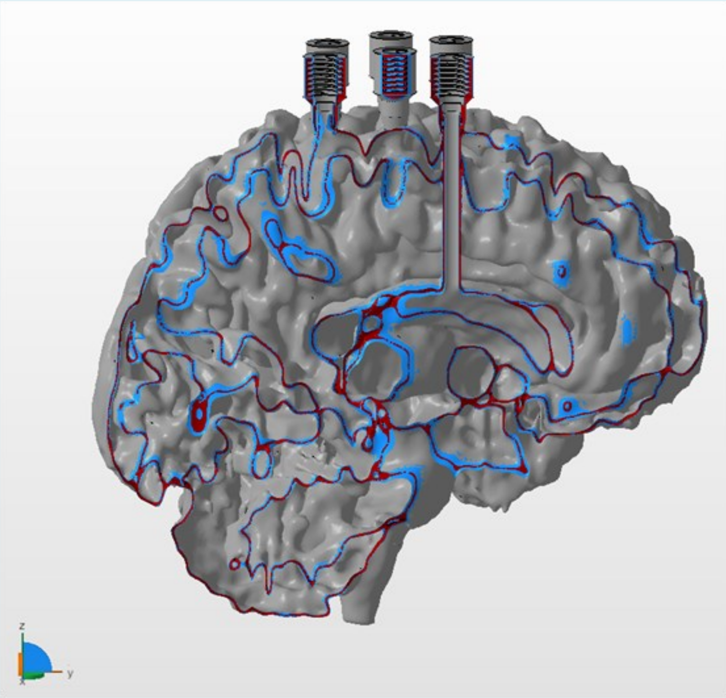
3D PRINTING

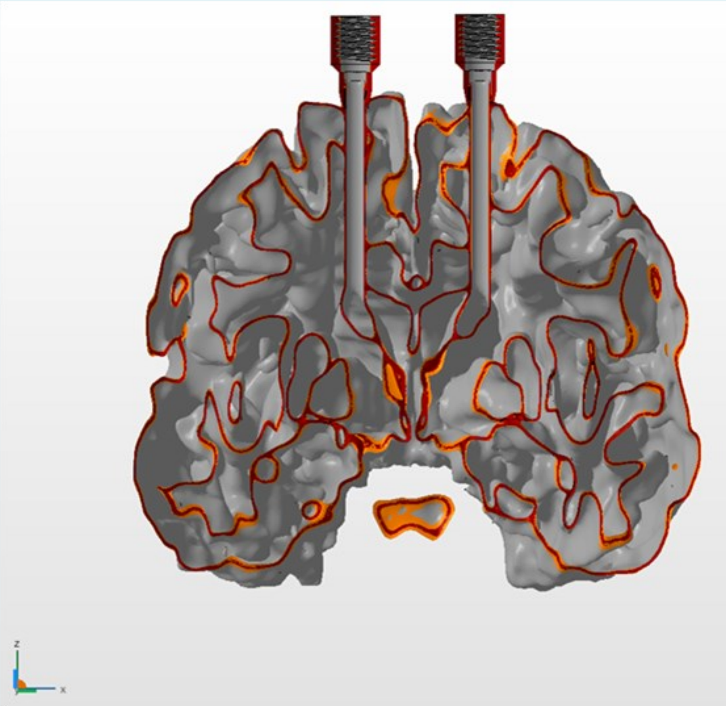
Ready to print?!

Methods

4 STL refinement





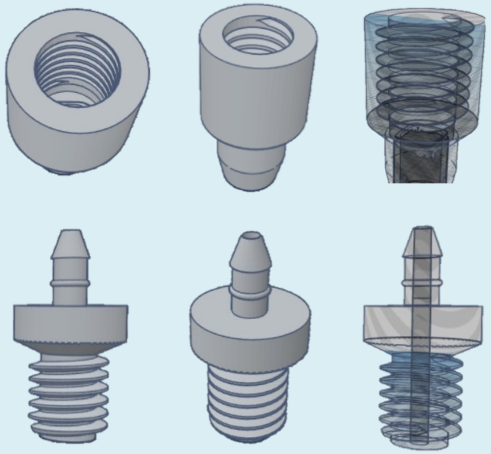


Methods

4 STL refinement

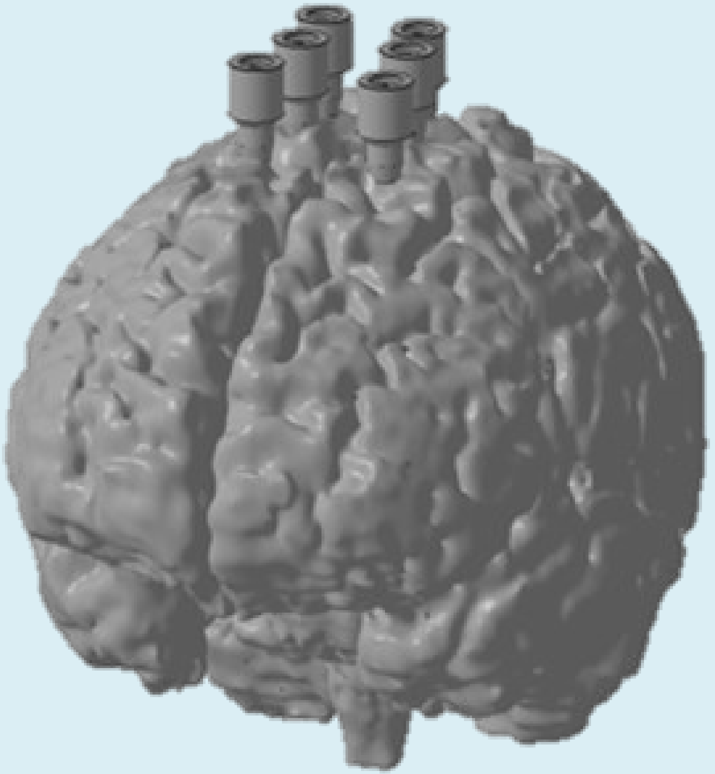
AUTODESK TINKERCAD

THREADED JOINTS
&
CAPS



AUTODESK NETFABB

STL REFINEMENT
&
CORRECTION



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3D PRINTING

Ready to print?!

7

WATERPROOFING

For filling with different solutions to simulate imaging modalities

8

FILLING SYSTEM

A special filling system for the brain phantom

5
6

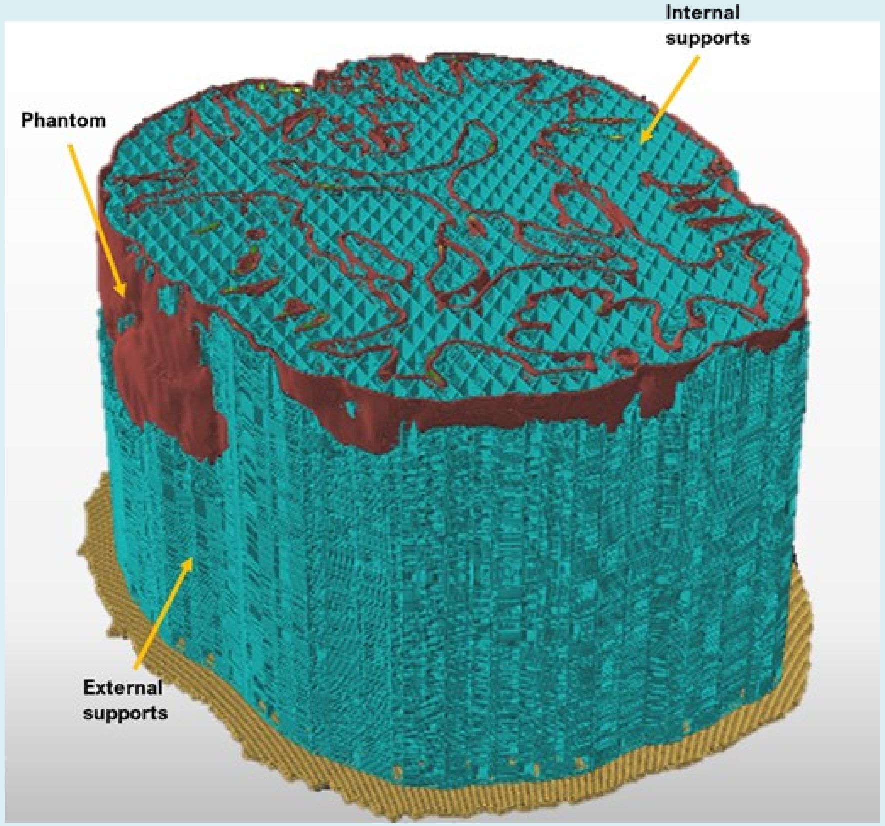
Slicing

STL model is sliced by means of a slicing software in a series of horizontal planed (slice or layers).

- Slicing defines the toolpath that the print head follows during printing to deposit layers one on top of the other;
- Supports structures are also generated automatically by slicing software.

SUPPORTS

- Are fundamental for the materialization of complex (and hollow) phantoms which contain protruding parts;
- Are printed in special soluble materials to be dissolved in the post-printing phase.



5 6

Slicing

In very complex anatomical phantoms, the quantity of support may grow very fast

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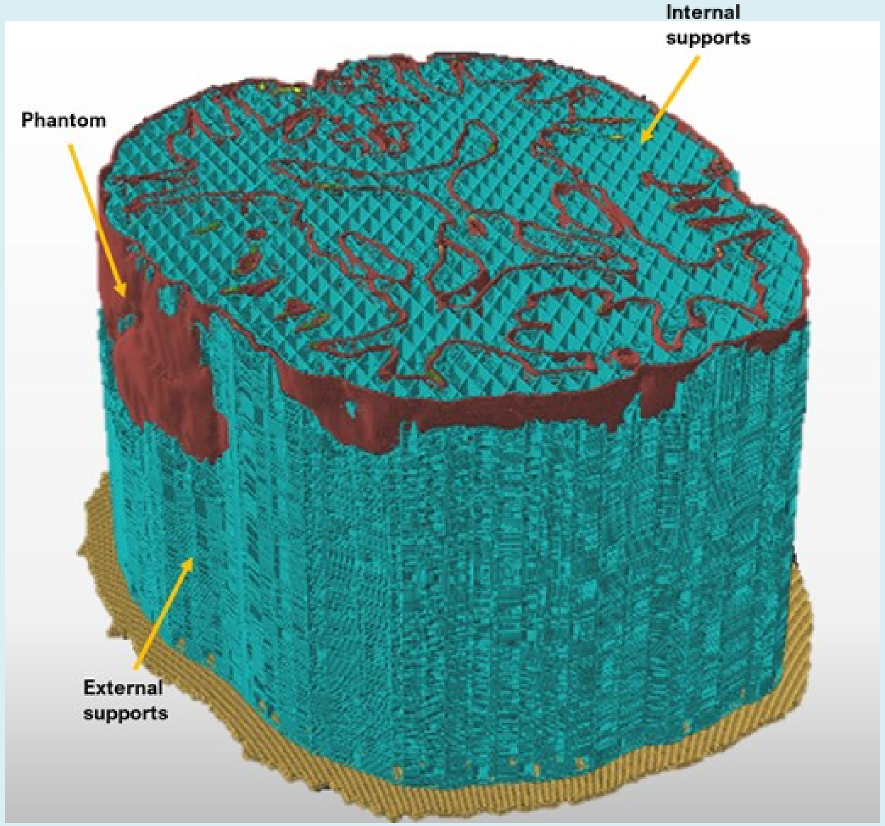
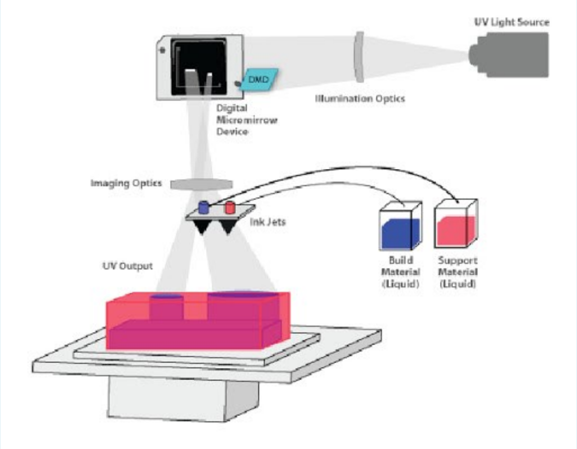


Prototyping

Choice of 3D Printing Technology

- Fused Deposition Modeling (FDM) and PolyJet (material jetting) are undoubtably the most widespread technologies to materialise 3D-printed anatomical phantoms.
- Although they provide similar advantages, FDM and PolyJet technologies are quite distinct and show different performances for 3DP of objects.

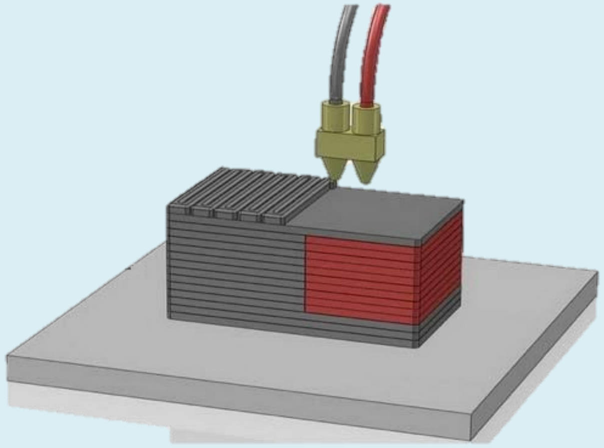


POLYJET

- surface finish
- precision
- fine details

FDM

- strength
- stability
- durability



M.A. Pirozzi, E. Andreozzi, M. Magliulo, P. Gargiulo, M. Cesarelli, B. Alfano, “3D-printed anatomical phantoms for medical imaging applications”, Proceedings of the 18th Nordic-Baltic Conference on Biomedical Engineering (NBC), Reykjavik, Iceland, 2020 (Article in press).

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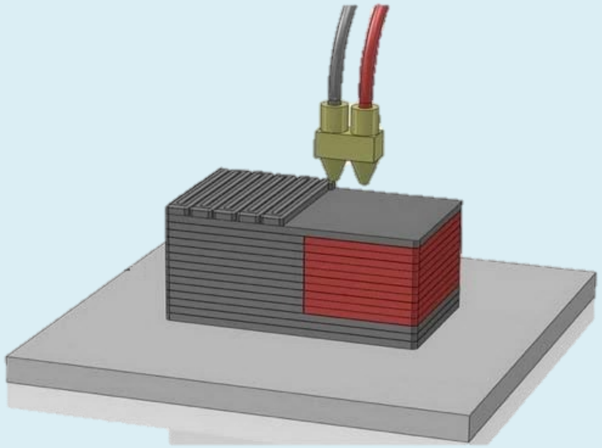

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Prototyping

56

Critical issues in the phantom print

1. The submillimeter wall thickness (0.5 mm), while manufacturers generally recommend it to be at least 1 mm, and impermeability.
2. The high number of efficient internal and external supports, in the critical points, completely removable at the end of printing.

Prototyping

5

6

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2. The high number of efficient internal and external supports, in the critical points, completely removable at the end of printing.

These problems arise both when choosing semi-professional and professional FDM 3D printers.

RAISE3D
RAISE THE STANDARD

RAISE3D N2 Plus

Semiprofessional 3D printer (FFF)

Stratasys F370

Professional 3D printer (FDM)

stratasys

itee Ph.D INFORMATION TECHNOLOGY ELECTRICAL ENGINEERING
UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II

Prototyping

5 6

Development with Semi-professional Printer

By optimizing the slicing parameters, we materialized a first rudimentary prototype of phantom, printed in PET-G (with non-removable supports), with submillimeter walls and an apparent impermeability.

56

Development with Semi-professional Printer

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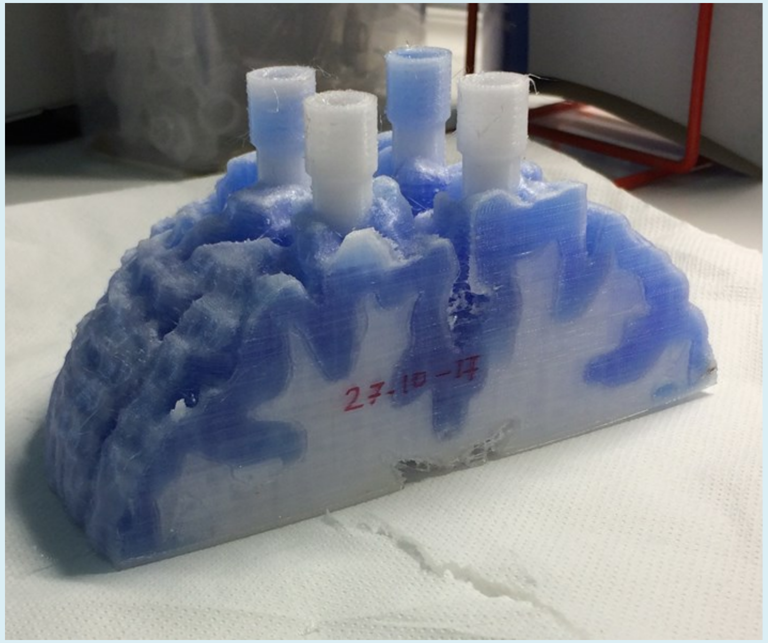
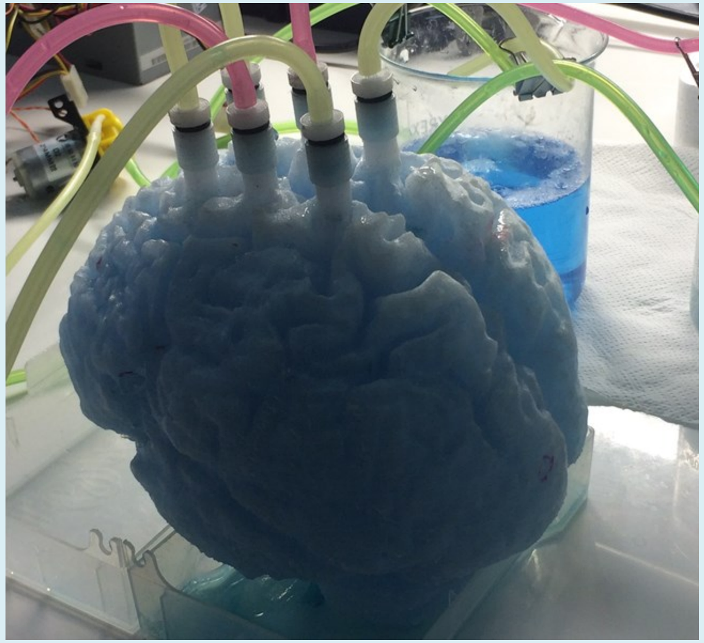
Printing Time

8 days and 16 hours

(1 extruder)





Prototyping

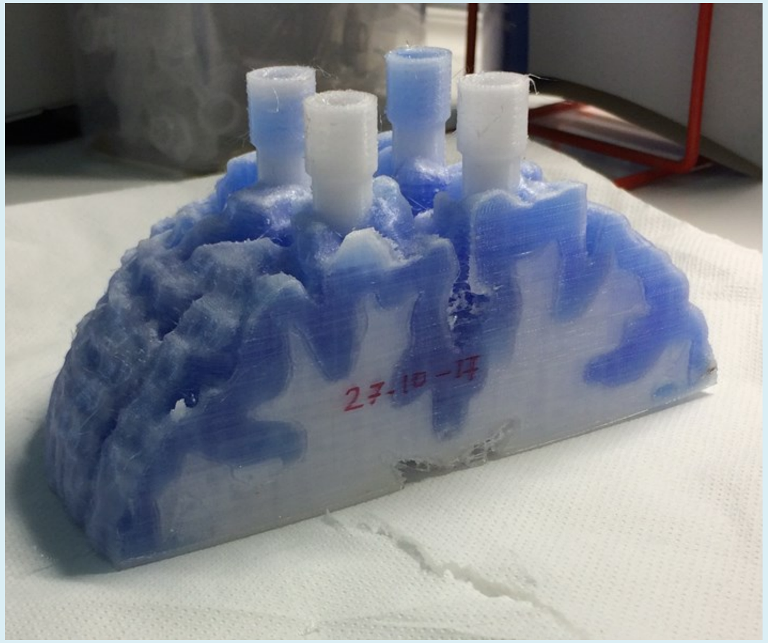
Development with Semi-professional Printer

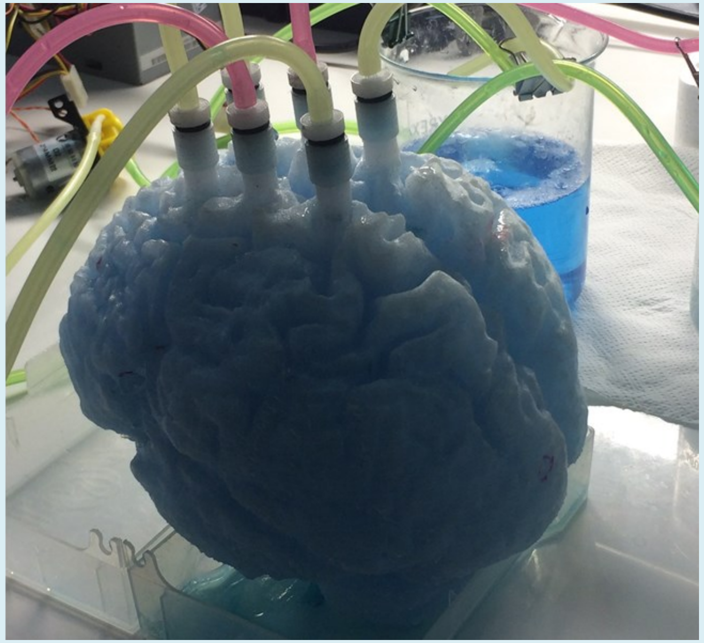
By optimizing the slicing parameters, we materialized a first rudimentary prototype of phantom, printed in PET-G (with non-removable supports), with submillimeter walls and an apparent impermeability.

Printing Time

(8 days and 16 hours) × 2

(2 extruder)





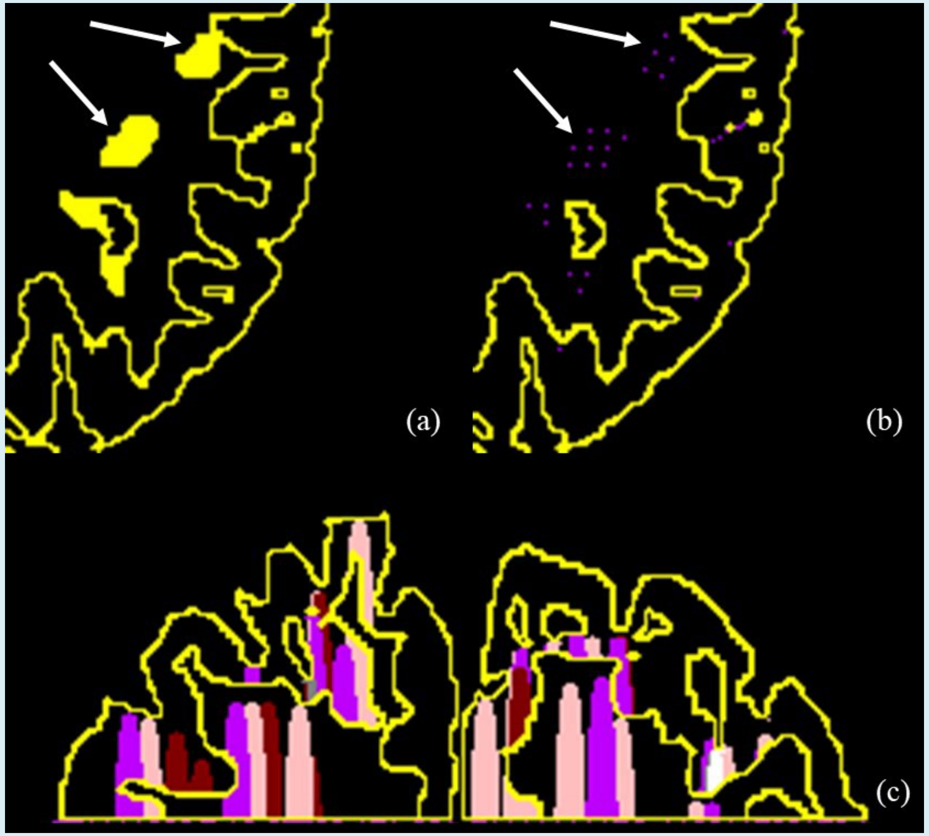
Prototyping

5 6

Development with Semi-professional Printer

Automatic method for the generation of efficient support structures for FDM 3DP of complex anthropomorphic phantoms:

- smaller amount of support material
- significant reduction in printing times compared to traditional support structures
- Faster dissolution of ad-hoc supports than traditional ones on the same piece



Prototyping

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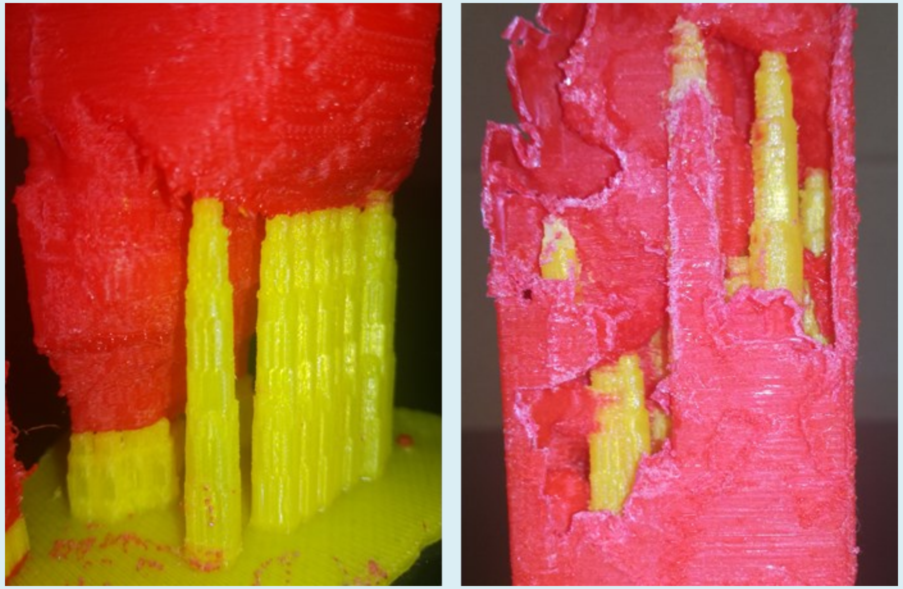
BUT…in not professional FDM 3DP

- interaction between the two extruders remains a difficult issue to manage
- materials suffer from the annoying problem of dripping, which makes them practically unusable for very long and complex prints.



M. A. Pirozzi, E. Andreozzi, M. Magliulo, P. Gargiulo, M. Cesarelli, and B. Alfano, "Automated Design of Efficient Supports in FDM 3D Printing of Anatomical Phantoms," in XV Mediterranean Conference on Medical and Biological Engineering and Computing – MEDICON 2019, Cham, 2020, pp. 292-300: Springer International Publishing.

5 6

Development with Professional Printer

Slicing parameters optimization through the advanced slicing software (Insight for GrabCAD) to be able to create walls with a minimum thickness of 0.5 mm that are robust and at the same time waterproof.

REQUIREMENTS FOR ROBUSTNESS

Where the wall thickness (horizontal or vertical) is minimum and equal to 0.5 mm:

- at least two juxtaposed vertical walls
- at least two overlapping horizontal layers

REQUIREMENTS FOR WATERPROOFING

The printing weft must be very dense with:

- minimal micro-porosity
- air-gaps in the walls reduced to a minimum

56

Development with Professional Printer

3DP material chosen for 3DP is ABS, which has a specific material for printing soluble supports (QSR support).

LAYER HEIGHT (LH) SETTING

- On Stratasys systems the available LH are 0.3302 mm, 0.2540 mm, 0.1778 mm and 0.1270 mm
- The best compromise solution for phantom requirements is LH = 0.1778 mm

56

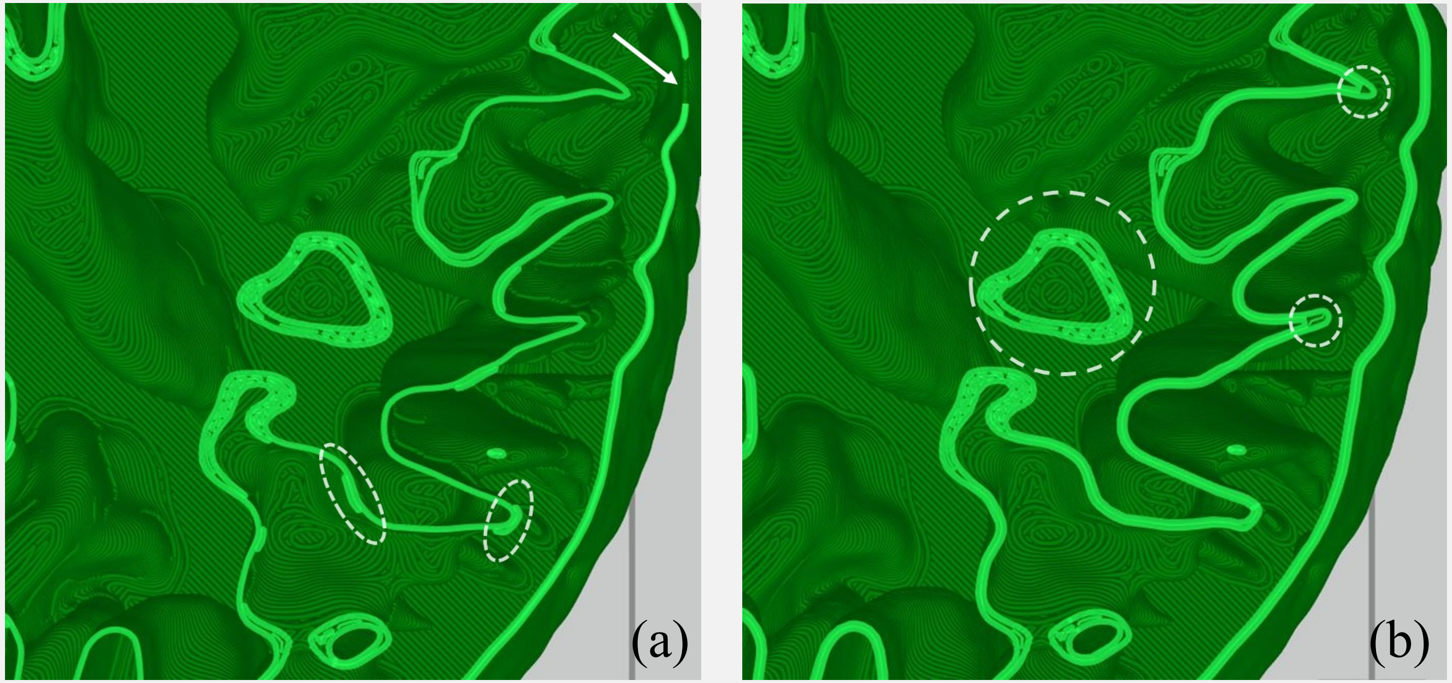
Development with Professional Printer

3DP material chosen for 3DP is ABS, which has a specific material for printing soluble supports (QSR support).

LAYER HEIGHT (LH) SETTING

(a) LH = 0.2540 mm

(b) LH = 0.2450 mm with option to thicken walls active



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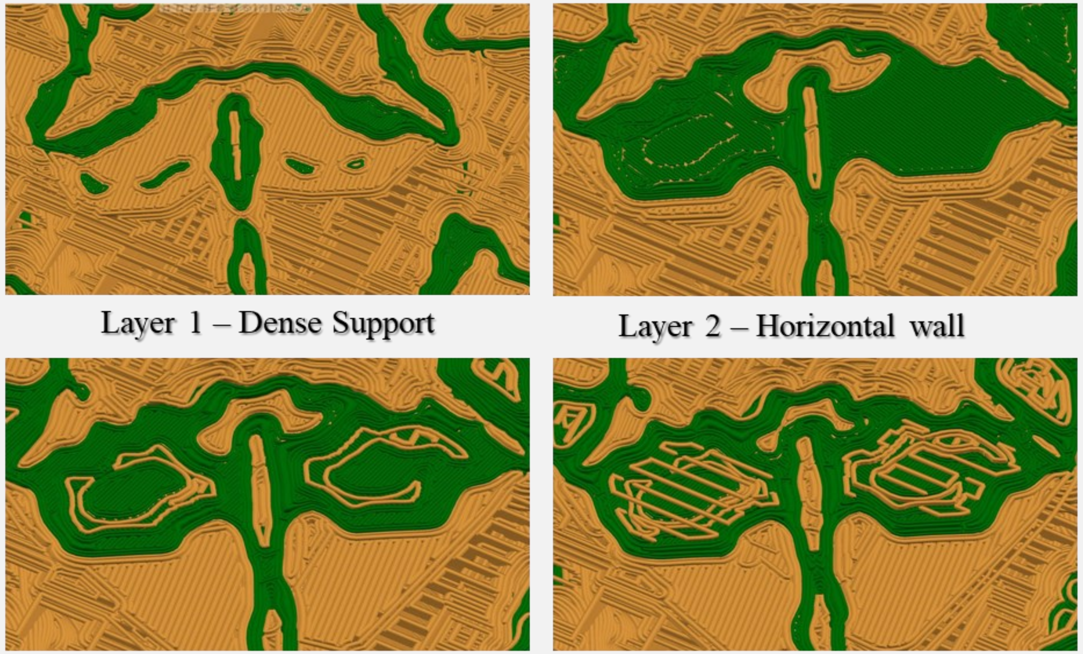

Layer 1 – Dense Support

Layer 2 – Horizontal wall

Layer 3 – Support structures

Layer 4 – Support structures

Development with Professional Printer

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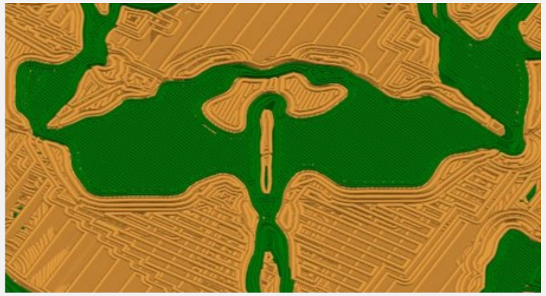


Layer 2 – Horizontal wall

Layer 3 – Horizontal wall

Layer 4 – Support structures

Prototyping

56

Development with Professional Printer

3DP material chosen for 3DP is ABS, which has a specific material for printing soluble supports (QSR support).

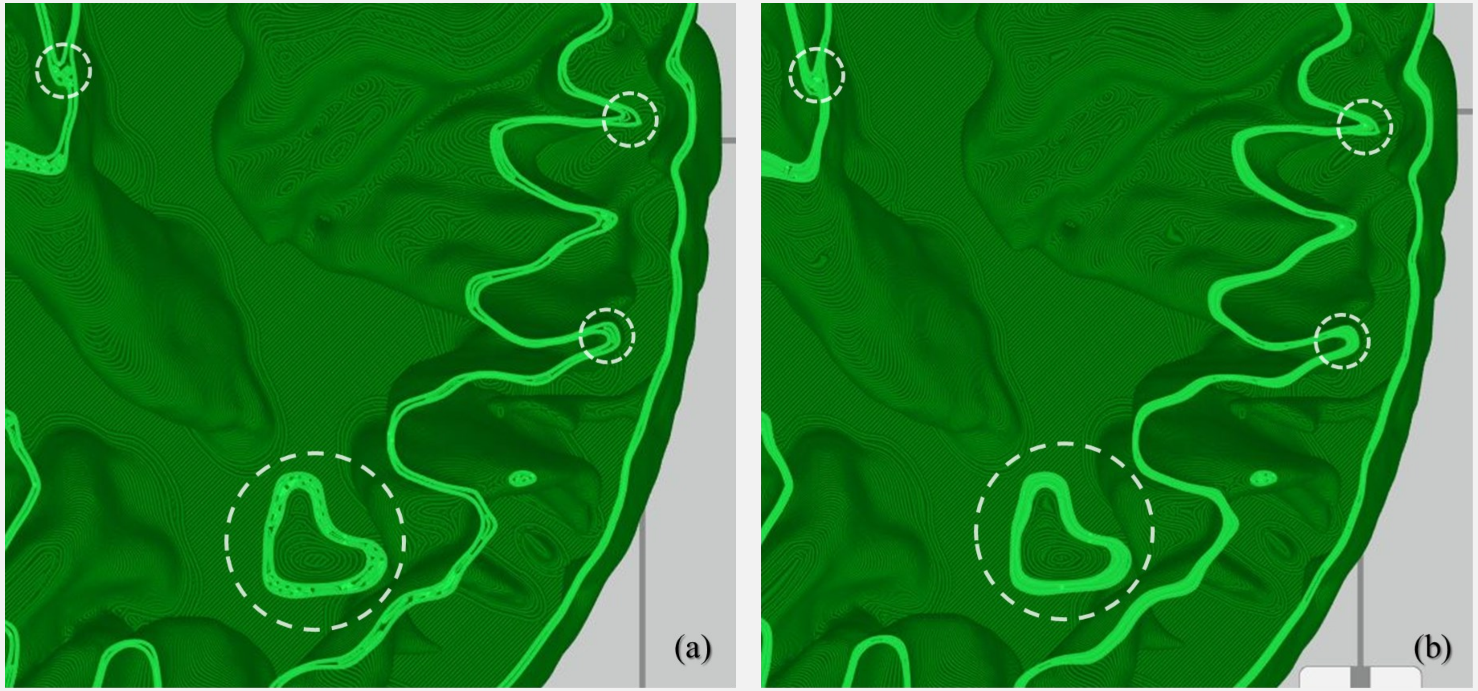
LAYER HEIGHT (LH) SETTING

(a) LH = 0.1778 mm with option to thicken walls active

↓

2 juxtaposed vertical walls (= 2 × LH thick)

(b) Advanced optimization of printing parameters to reduce air-gaps



Prototyping

Development with Professional Printer

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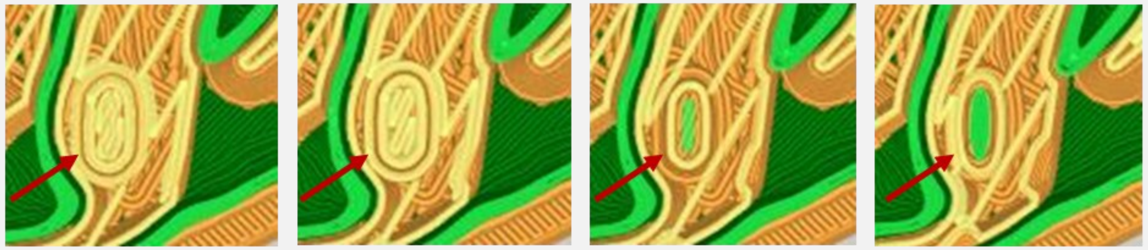
SUPPORTS OPTIMIZATION

(a) SMART supports

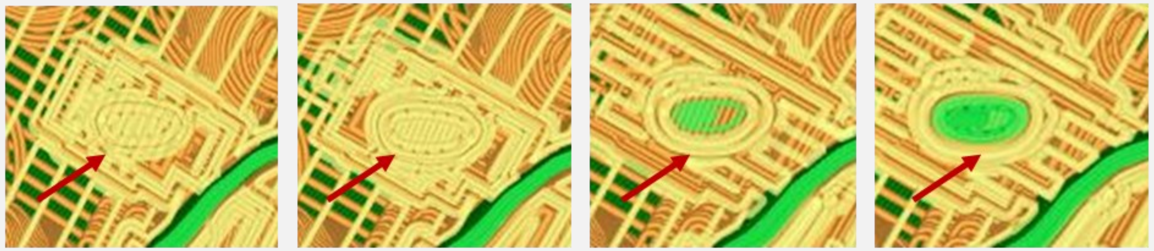
(b) Dense support layer

Critical point (A)



(A.1) (A.2) (A.3) (A.4)

Critical point (B)



(B.1) (B.2) (B.3) (B.4)

Prototyping

5 6

Development with Professional Printer

3DP material chosen for 3DP is ABS, which has a specific material for printing soluble supports (QSR support).

SUPPORTS OPTIMIZATION

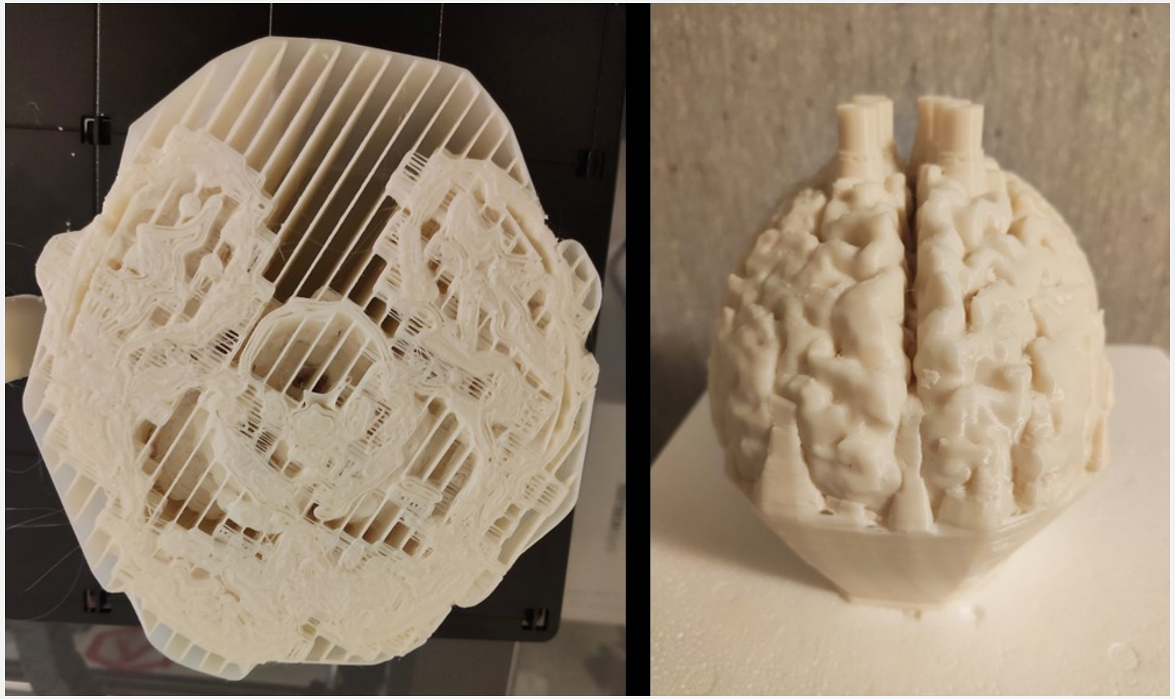
(a) SMART supports

(b) Dense support layer

Printing Time

7 days and 3 hours

(2 extruder)

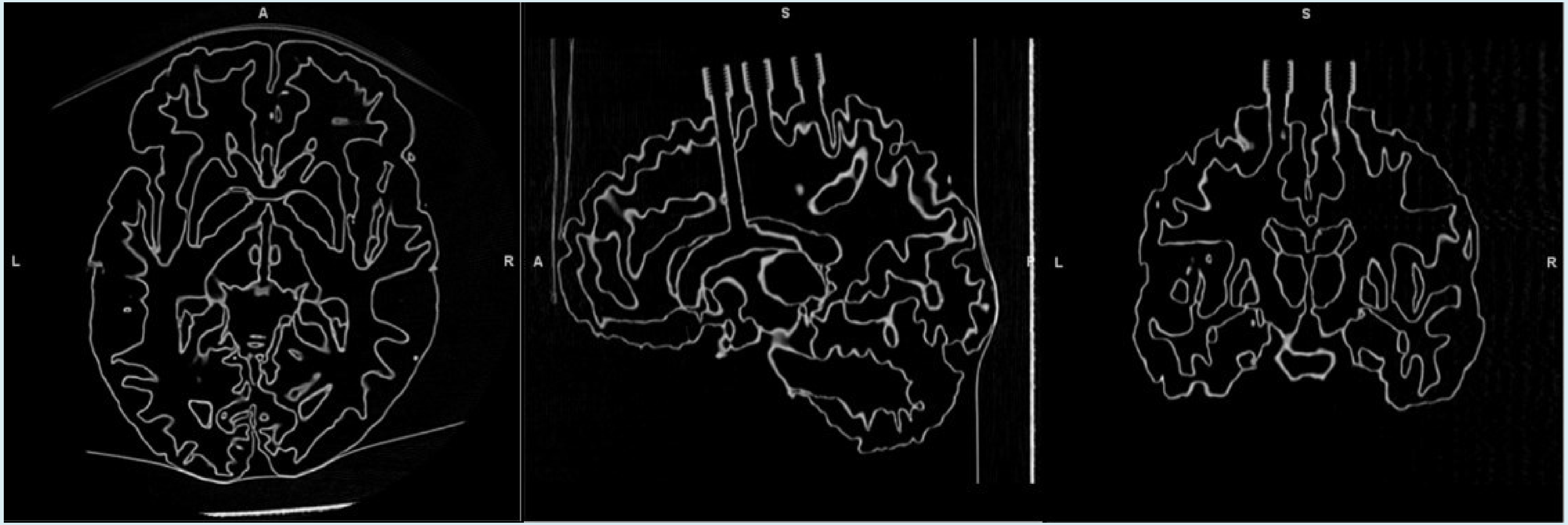


Prototyping

56

Removal of Soluble Supports

The FDM washing system Support Cleaning Apparatus (SCA-1200HT) allow the removal of all internal supports



Prototyping

Developments

5

SLICING

STL model is sliced by means of slicing software

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3D PRINTING

Ready to print?!

7

WATERPROOFING

For filling with different solutions to simulate imaging modalities

8

FILLING SYSTEM

A special filling system for the brain phantom

Prototyping

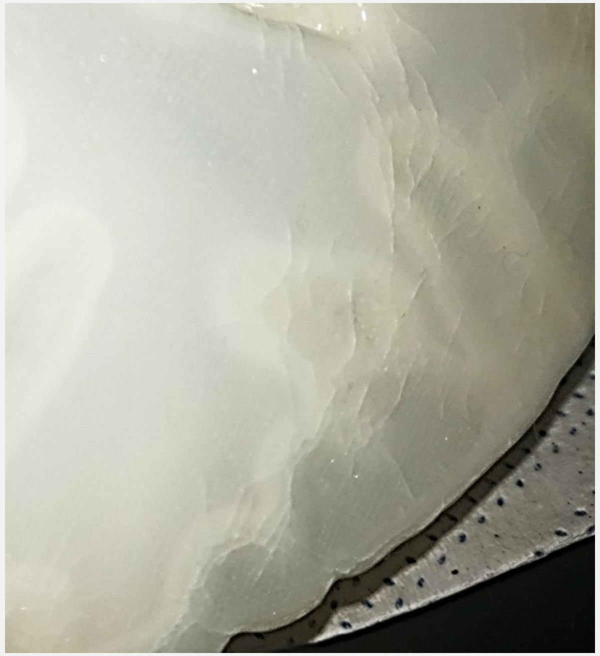
7 Waterproofing

WITH ACETONE

Prototyping

7 Waterproofing

WITH ACETONE

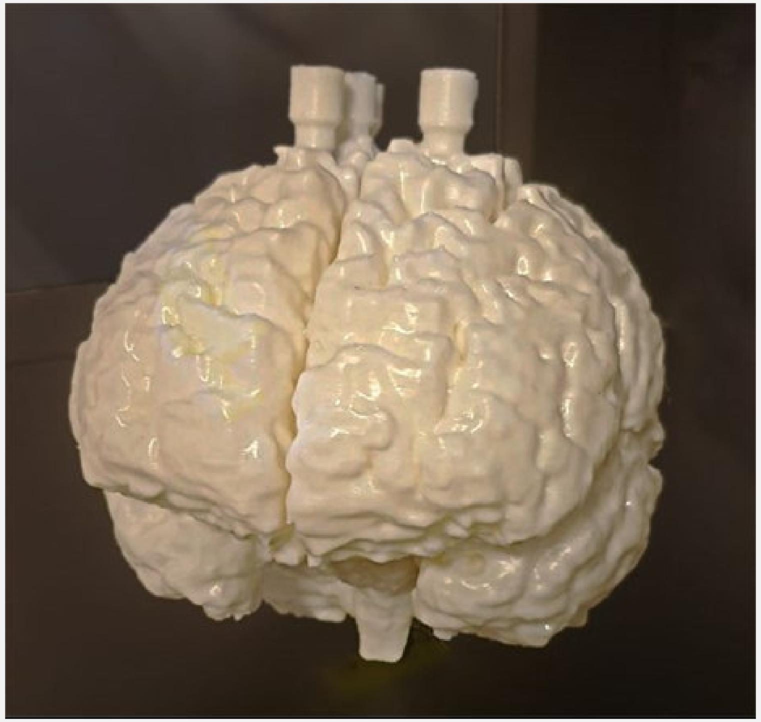


Damage to the ABS walls after repeated treatments with acetone

7 Waterproofing

WITH POLYVINYL-ACETATE

- Solution of water and polyvinyl acetate (20% and 80% of the total volume)
- The solution penetrates the print texture by physically closing the micropores in the printed surfaces
- Effective waterproofing: no passage of liquids towards the outside and between the compartments of the phantom



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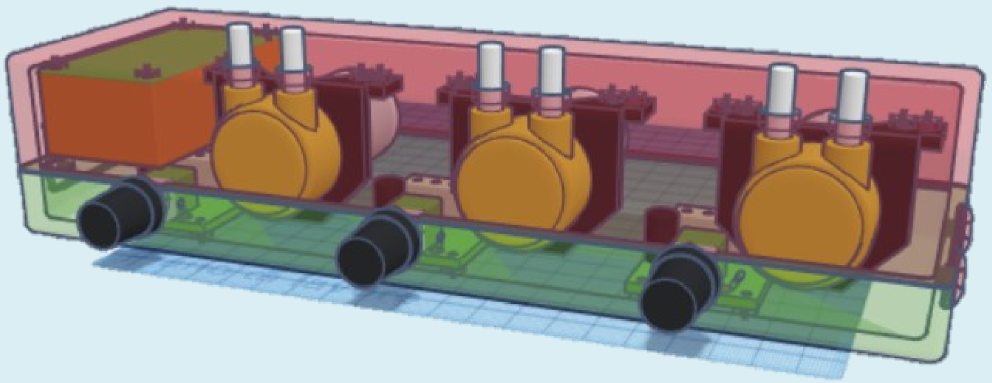
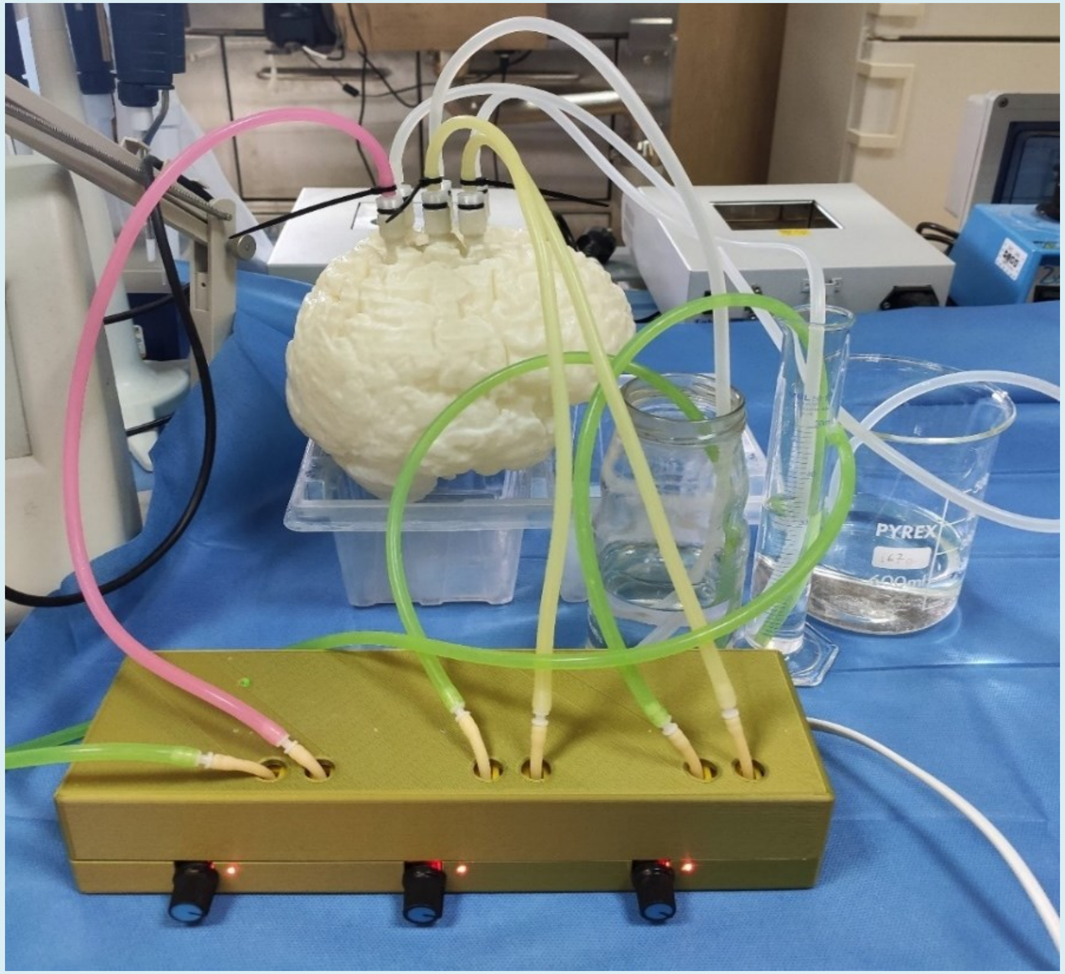
8 Filling setup

Filling system for the escape of air bubbles that could become trapped in the phantom and cause areas of hypo-intensity on imaging.

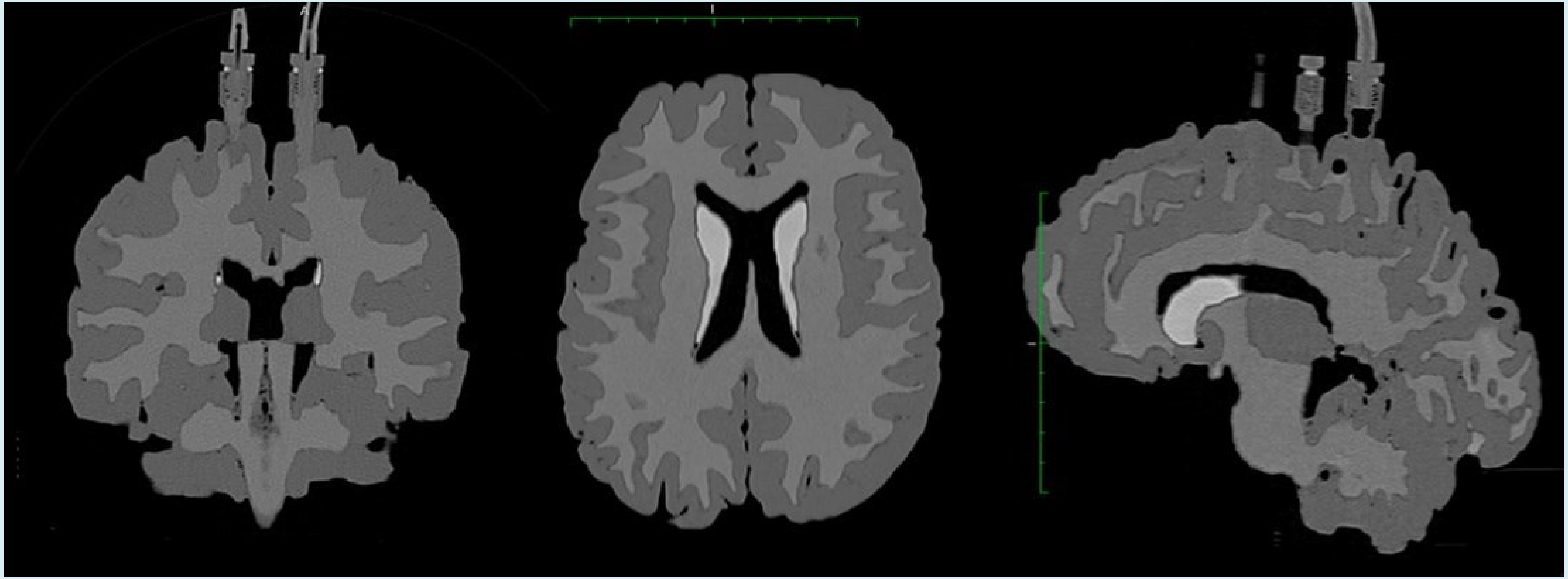




Prototyping

8 Phantom scans

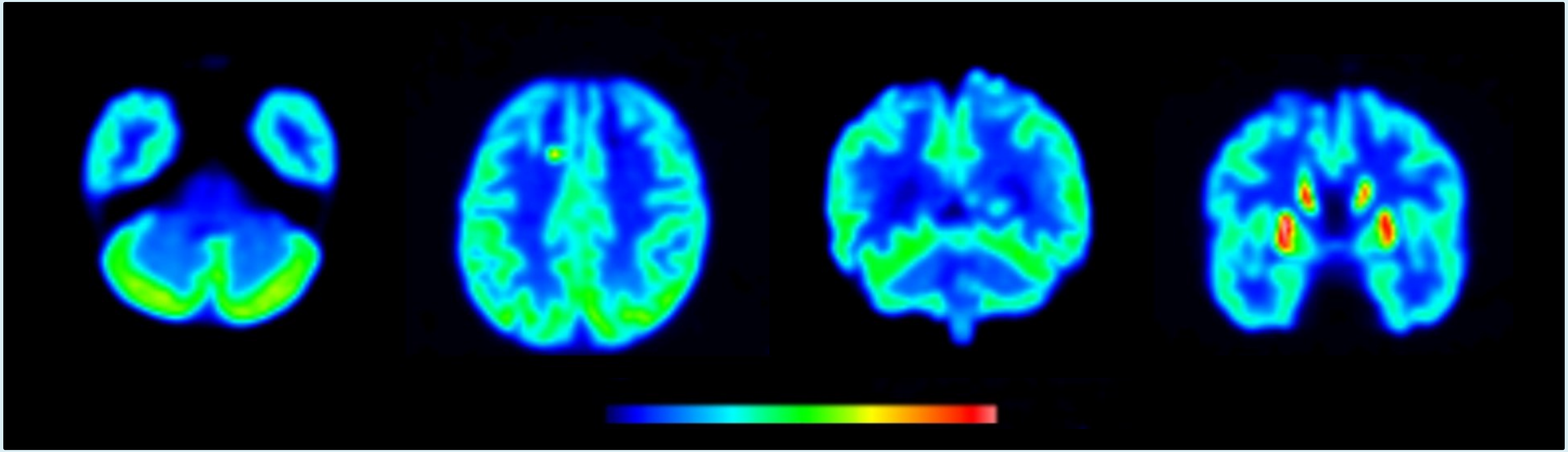
CT scan with different concentration of contrast medium



Prototyping

8 Phantom scans

Pet/CT scan with different concentration of radioactive tracer ^{18}F-FDG



Bases for Future Developments: a New Approach for Multiparametric Brain Segmentation

Bases for Future Developments

Improvement of the 3D Modelling

- Phantomag has limitation for 3D modelling related to image resolution, to be overcome in future versions of the anthropomorphic brain phantom.
- Brain phantom customization

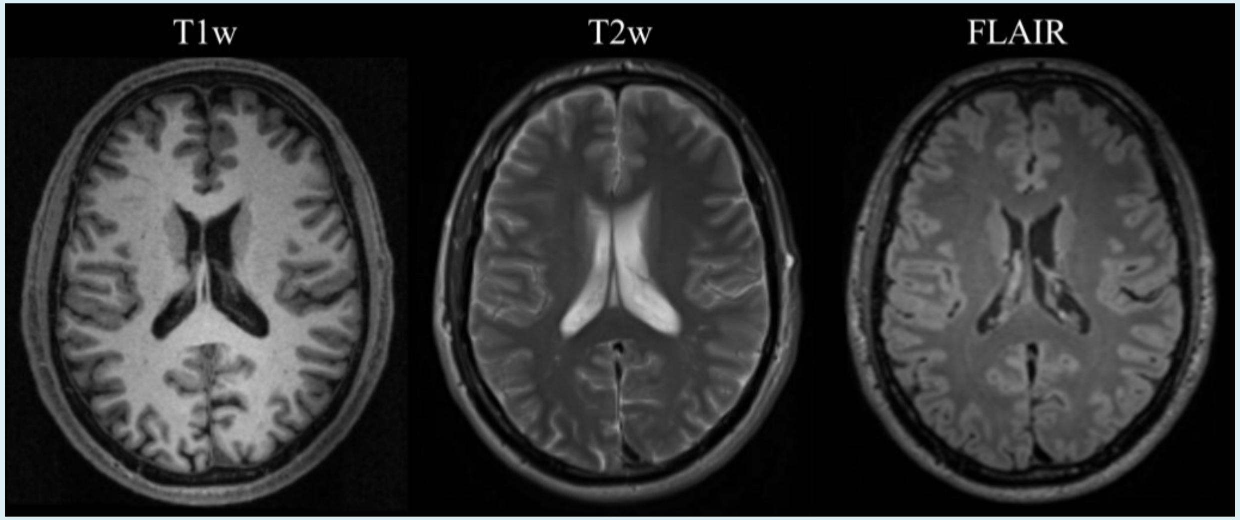
Brain Segmentation for 3DP

?

Bases for Future Developments

Brain Segmentation

- Most automatic brain segmentation software segments only GM, WM, and CSF
- Basal nuclei are usually segmented by hand by experienced neuro-radiologists
- Specially designed packages are typically added to the general framework to automatically segment subcortical structures, basal nuclei and lesions
- Most brain segmentation methods are designed to work on T1w, T2w or even FLAIR images, and therefore on MRI signal intensities



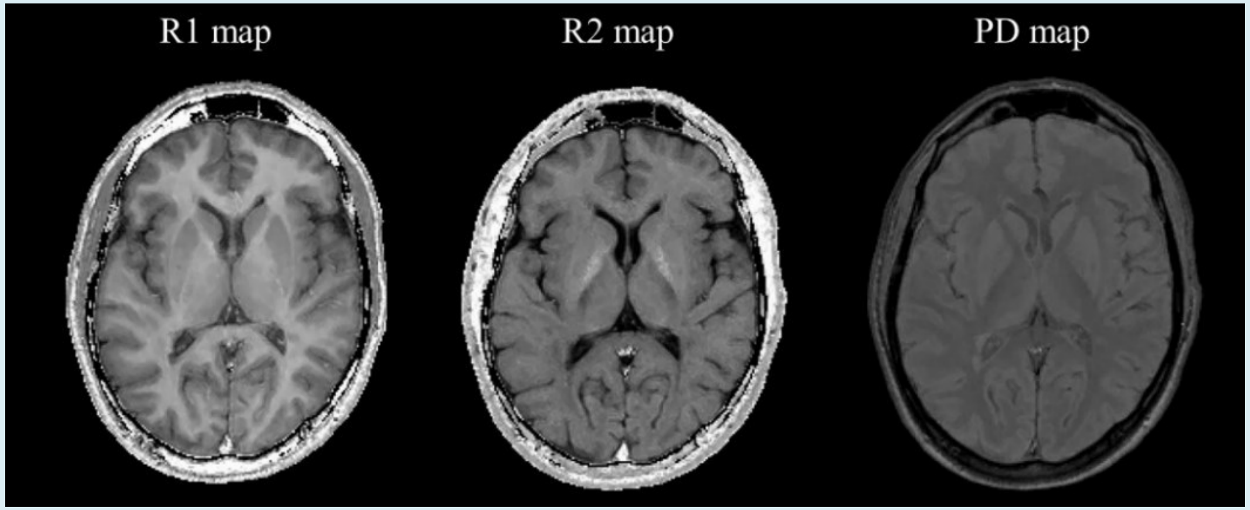
Routine clinical MRI protocols (3D-GrE T1w, FLAIR and fast-T2w sequences with ≤ 3 mm slice thickness)

Bases for Future Developments

Brain Segmentation based on relaxometry

MRI relaxation parameters:

- R1 = 1/T1, Longitudinal Relaxation Rate
- R2 = 1/T2, Transversal Relaxation Rate
- PD, Proton Density



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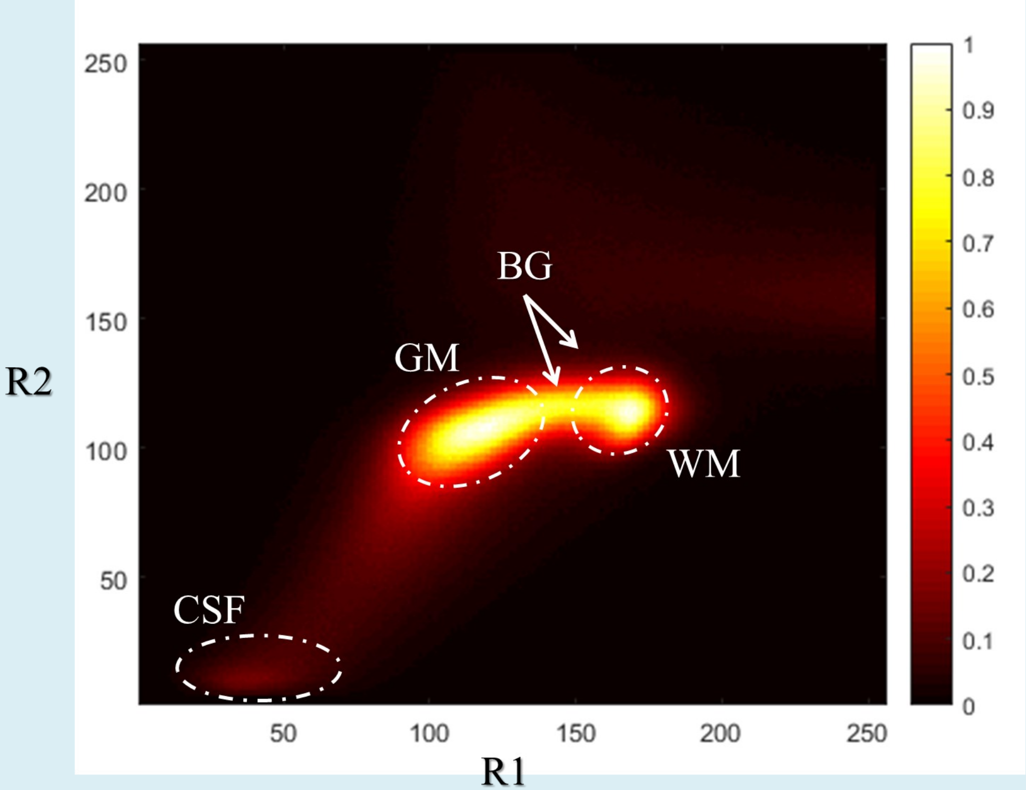
- R2 = 1/T2, Transversal Relaxation Rate
- PD, Proton Density

Relaxation rate maps provide a reproducible position of the voxel clusters of brain tissues in the multi-parametric space.



B. Alfano *et al.*, "Unsupervised, automated segmentation of the normal brain using a multispectral relaxometric magnetic resonance approach," *Magnetic Resonance in Medicine*, https://doi.org/10.1002/mrm.1910370113 vol. 37, no. 1, pp. 84-93, 1997/01/01 1997.

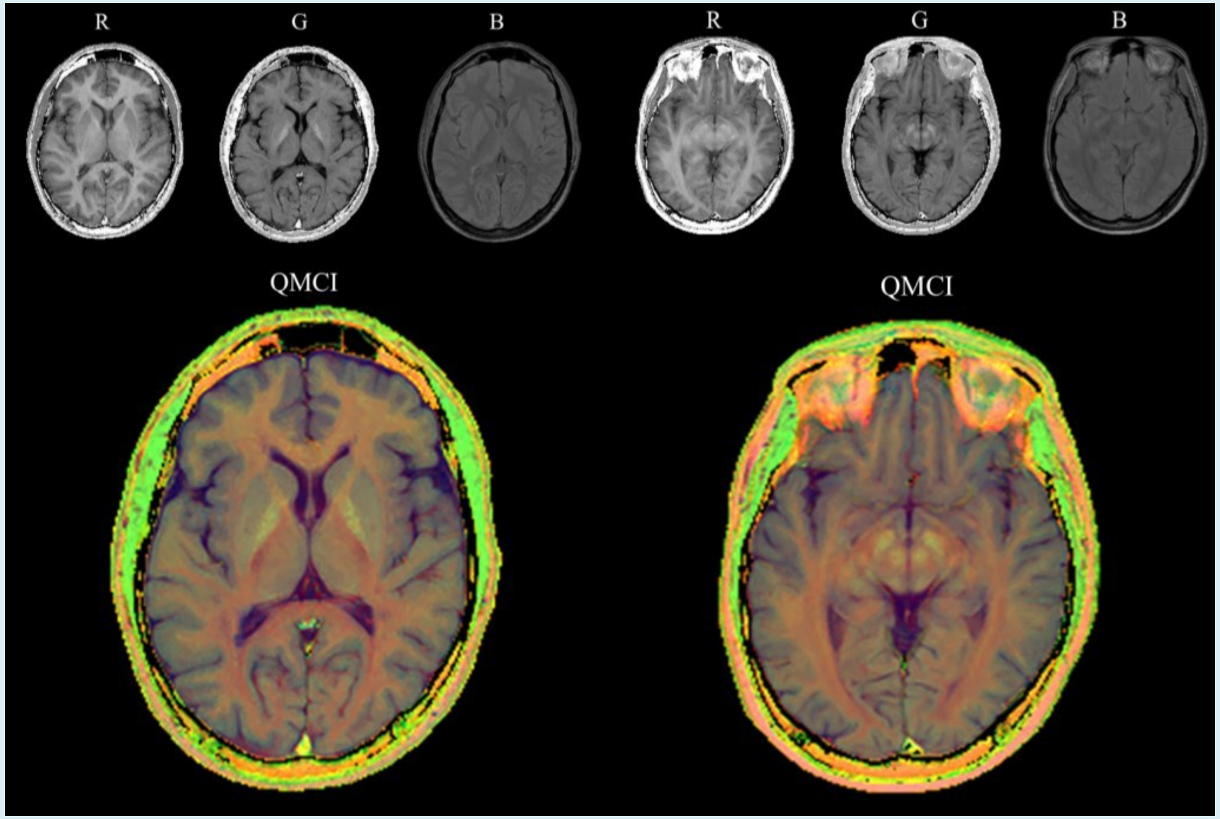
Bases for Future Developments

Brain Segmentation based on relaxometry

MRI relaxation parameters:

- R1 = 1/T1, Longitudinal Relaxation Rate
- R2 = 1/T2, Transversal Relaxation Rate
- PD, Proton Density

Quantitative Magnetic Color Imaging (QMCI) to simultaneously display three relaxation parameters (R1, R2 , PD) with a full-color approach.



B. Alfano, A. Brunetti, M. Arpaia, A. Ciarmiello, E. M. Covelli, and M. Salvatore, "Multiparametric display of spin-echo data from MR studies of brain," Journal of Magnetic Resonance Imaging, https://doi.org/10.1002/jmri.1880050218 vol. 5, no. 2, pp. 217-225, 1995/03/01 1995.

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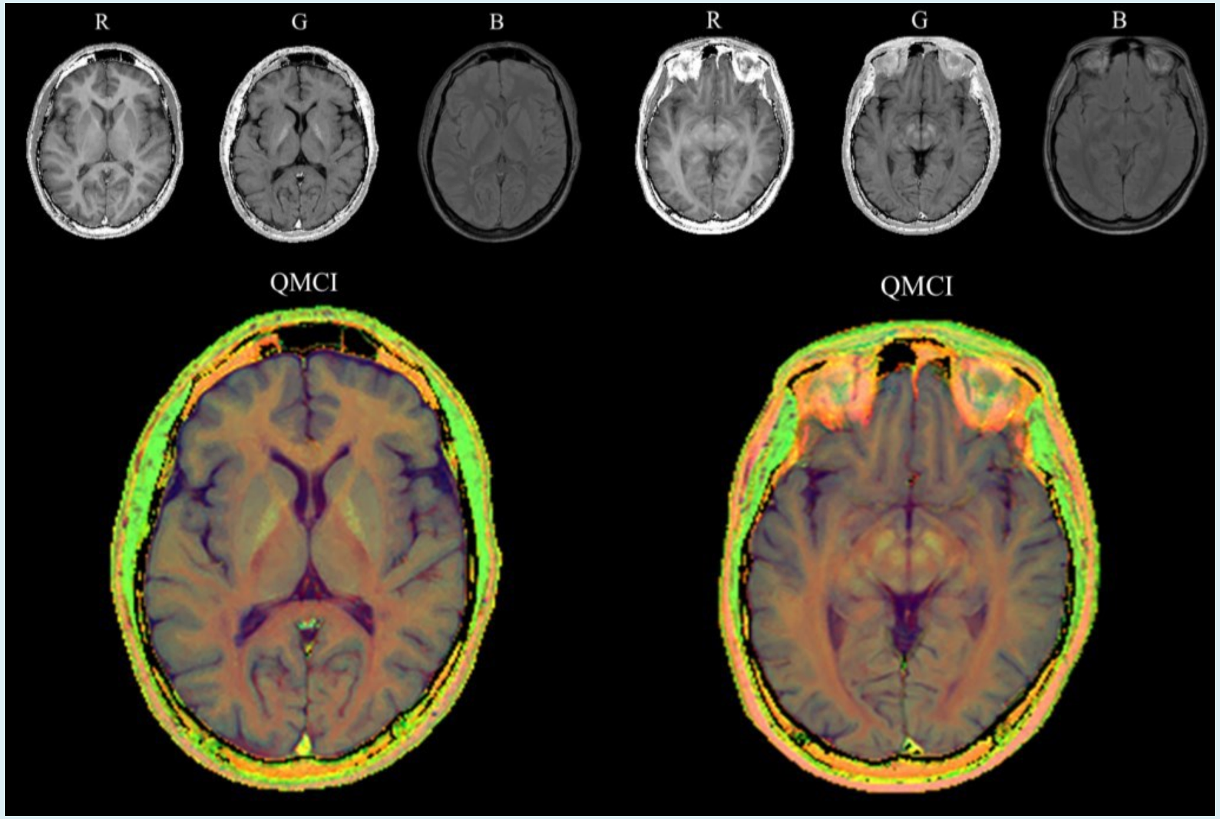
These maps were calculated from spin-echo data obtained by Conventional Spin-Echo (CSE) acquisitions no longer used in clinical practice due to long acquisition times.



B. Alfano, A. Brunetti, M. Arpaia, A. Ciarmiello, E. M. Covelli, and M. Salvatore, "Multiparametric display of spin-echo data from MR studies of brain," Journal of Magnetic Resonance Imaging, https://doi.org/10.1002/jmri.1880050218 vol. 5, no. 2, pp. 217-225, 1995/03/01 1995.

Bases for Future Developments

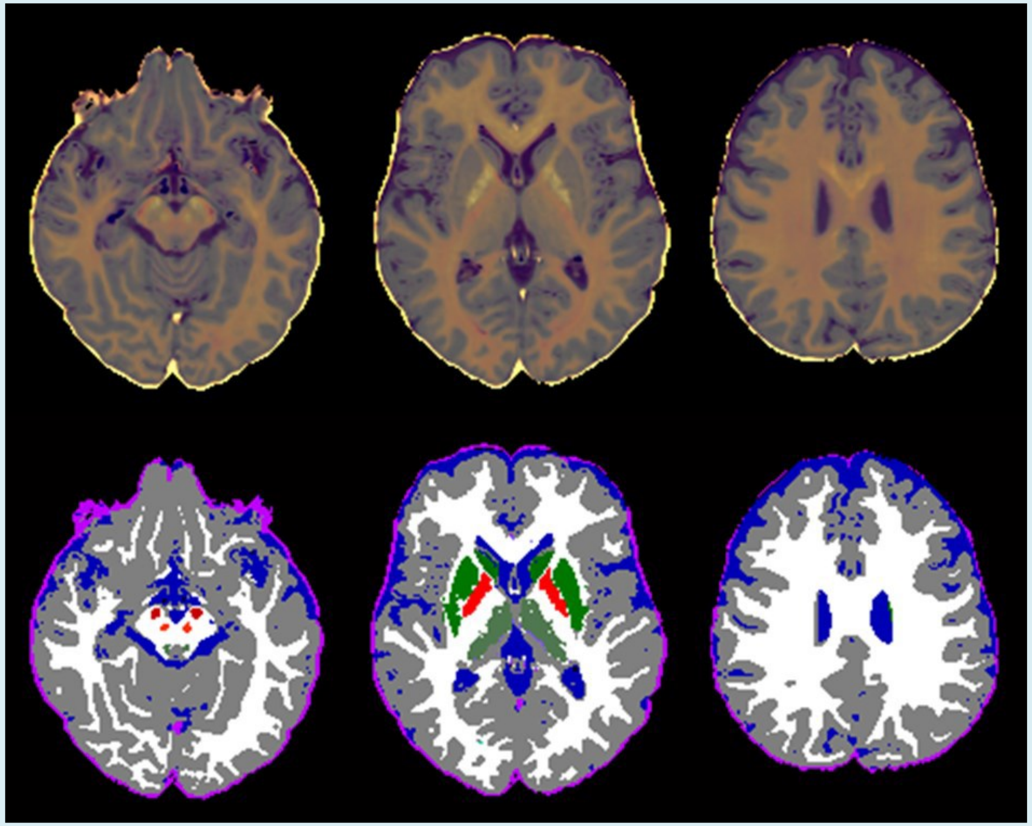
Relaxation rate maps estimation

***M.A. Pirozzi**, M. Tranfa, M. Tortora, R. Lanzillo, V. Brescia Morra, A. Brunetti, B. Alfano, M. Quarantelli, "A polynomial regression-based approach to estimate relaxation rate maps suitable for multiparametric segmentation of clinical brain MRI studies in multiple sclerosis.". [Under Review - Medical Image Analysis journal].*

Bases for Future Developments

The New Approach

- A new multiparametric brain segmentation approach based on pseudo-relaxation parameter maps
- Segmentation of main brain tissues GM, WM and CSF
- Segmentation of thalamus and basal ganglia (caudate nucleus, putamen, pallidus, nigra, red nucleus, dentate)
- Adaptable to different acquisition sequences
- Suitable for 3DP



__M.A. Pirozzi__, M. Tranfa, M. Tortora, R. Lanzillo, V. Brescia Morra, A. Brunetti, B. Alfano, M. Quarantelli, "A polynomial regression-based approach to estimate relaxation rate maps suitable for multiparametric segmentation of clinical brain MRI studies in multiple sclerosis.". [Under Review - Medical Image Analysis journal].

Bases for Future Developments

The New Approach

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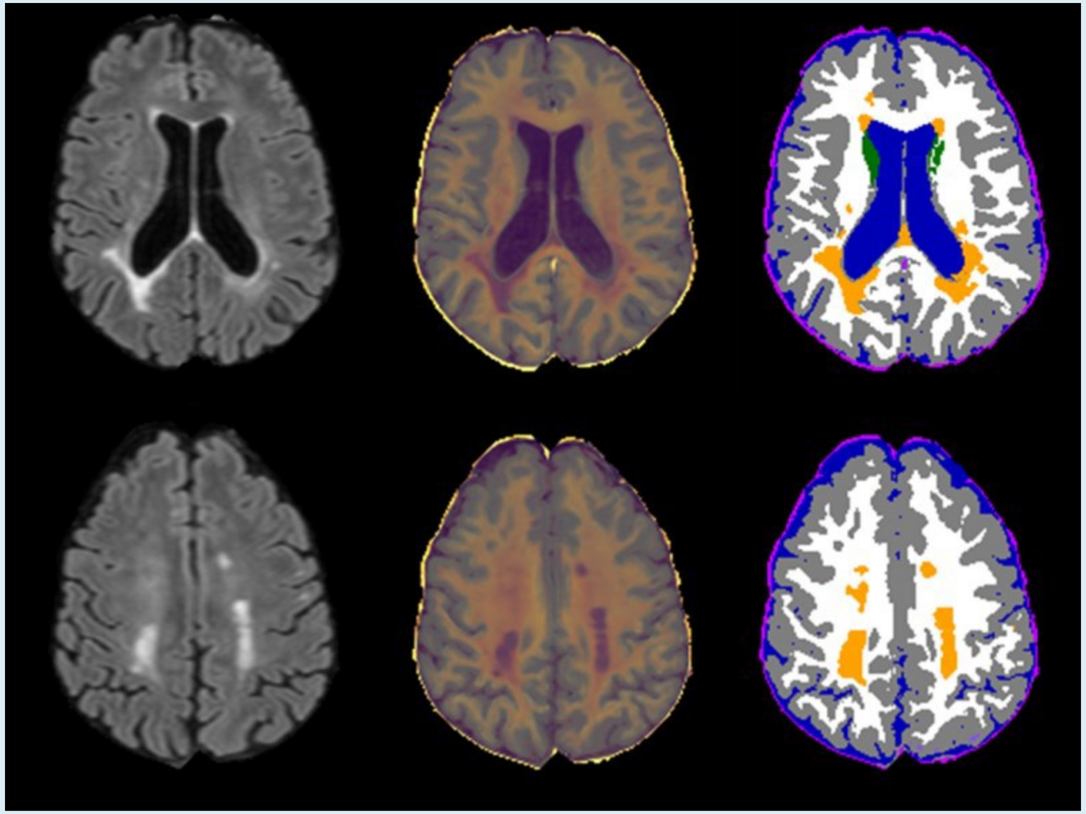
- Segmentation of thalamus and basal ganglia (caudate nucleus, putamen, pallidus, nigra, red nucleus, dentate)
- Adaptable to different acquisition sequences
- Suitable for 3DP
- Segmentation of the WM lesions due to multiple sclerosis



__M.A. Pirozzi__, M. Tranfa, M. Tortora, R. Lanzillo, V. Brescia Morra, A. Brunetti, B. Alfano, M. Quarantelli, "A polynomial regression-based approach to estimate relaxation rate maps suitable for multiparametric segmentation of clinical brain MRI studies in multiple sclerosis.". [Under Review - Medical Image Analysis journal].

Conclusion

Towards custom 3D-printed phantoms…

- Compared to the state-of-the-art, the new STEPBrain phantom has several potential advantages. Having separate compartments, it can simulate 3 different compartments, simultaneously, to perform tests with different imaging methods, simply by changing the filling solution.
- The development of innovative techniques to devise anthropomorphic phantom is expected to increase in the future, given the growing interest in multi-modal and multi-parametric imaging modalities (PET/CT, PET/MRI).
- Consequently, the effort aimed at customizing modeling processes and developing of 3DP technology for these applications is expected to grow significantly in the coming years.
- The techniques already developed and could be extended to design anatomical phantoms of other organs, also towards greater product customization, through specific segmentation techniques for 3DP.

THANK YOU!

Questions?

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