Automated brain segmentation and volumetry in dementia diagnostics: a narrative review with emphasis on FreeSurfer

Eya Khadhraoui, Thomas Nickl-Jockschat, Hans Henkes, Daniel Behme and Sebastian Johannes Müller
(Clinic for Neuroradiology, University Hospital, Magdeburg, Germany)

Overview

- **Dementia** = syndrome associated with **many** neurodegenerative diseases (Alzheimer, mild cognitive impairment, frontotemporal dementia, Parkinson, Lewy bodies, etc.)
- 7th most common cause of death globally (WHO, 2021) (6 first leading causes of death in 2021?)
- Cause disability and dependency
- **Incidence** expected to increase with population aging
  - 10m new diagnosed patients per year worldwide
  - incidence doubles every 6.3-year increase in age (5% of the population older than 65, and 20–40% of those older than 85)

⇒ **early detection** (particularly volumetry from MRI) **and prevention**

- <u>**Goals**</u>**:**
1) Assess the current use of automated brain segmentation and volumetry in the field of dementia diagnosis (focus on FreeSurfer and Alzheimer's disease)
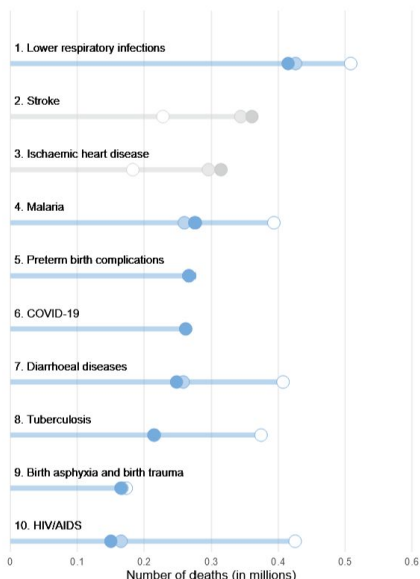2) Identify recommandations, gaps, and opportunities with brain MRI research

Leading causes of death in 2021 ? (WHO)

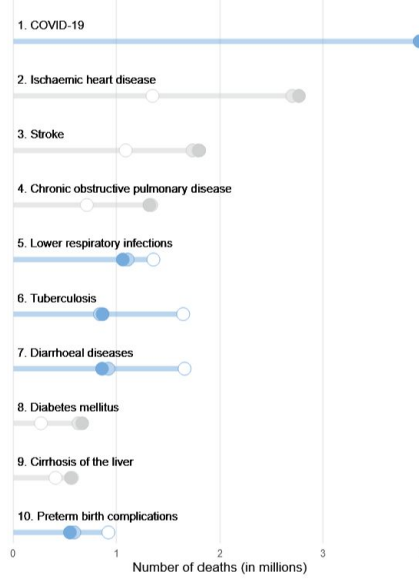Depends on the **country's level of income** !
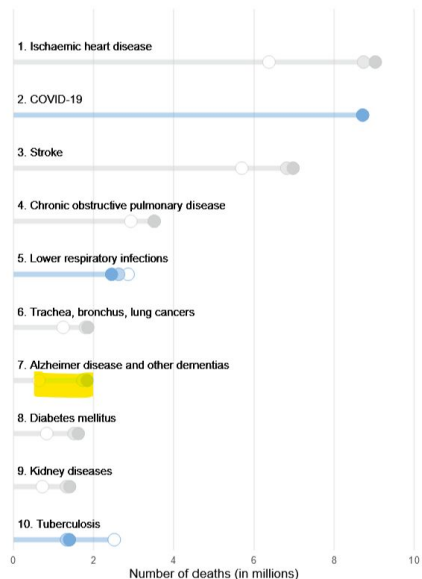
Source: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death
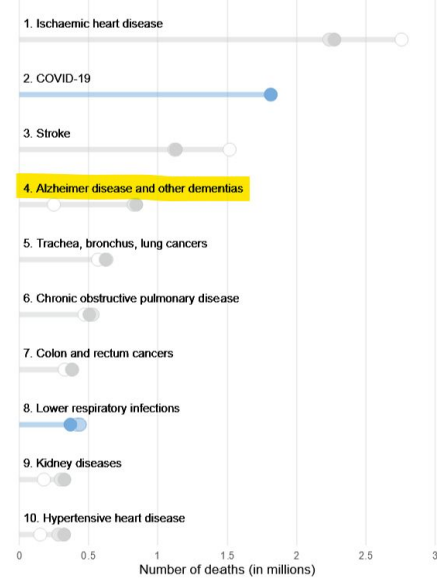
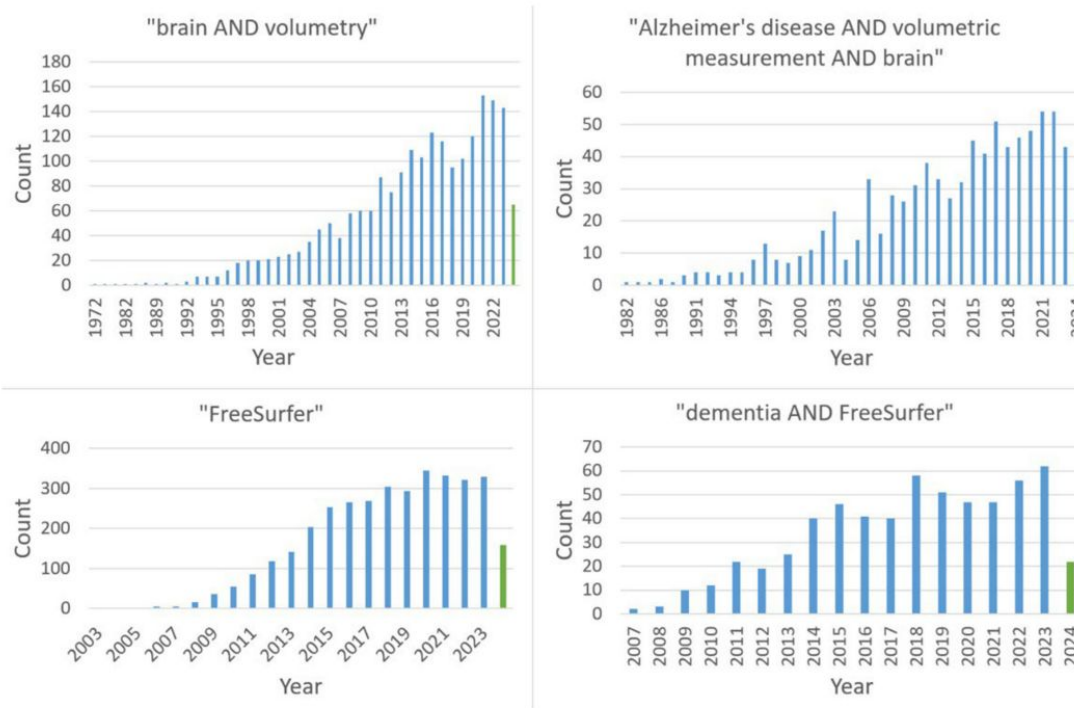# Method of selection of publications

FIGURE 1
The <mark>PubMed</mark> time line of the four relevant search terms (green: 2024).
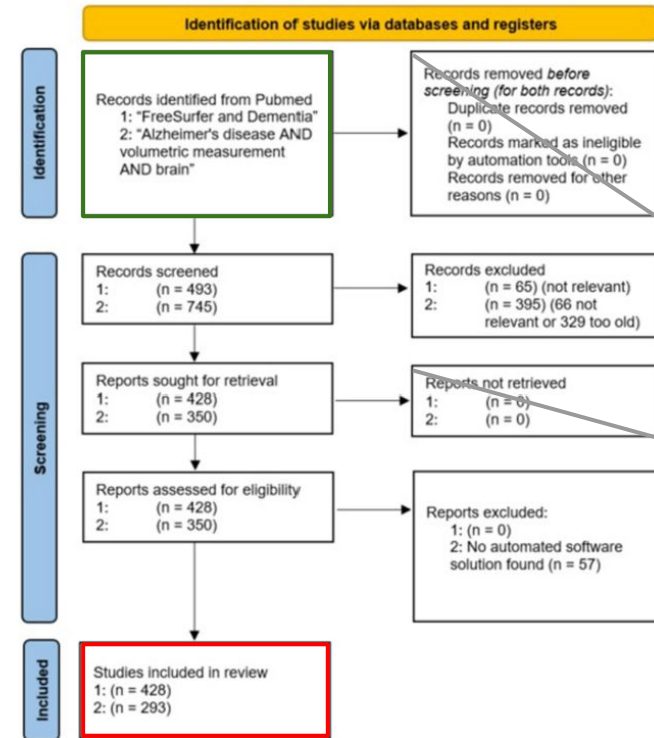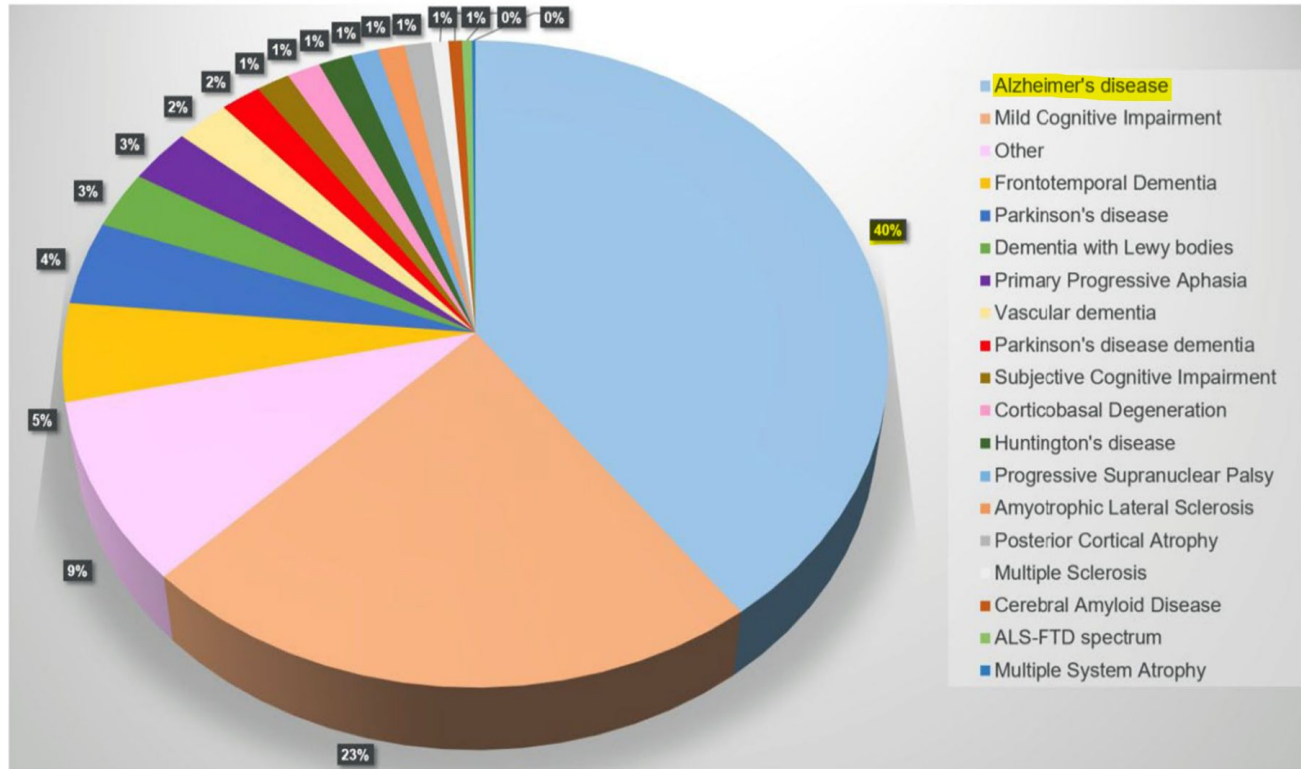
FIGURE 2
PRISMA flow chart of the included PubMed studies for both search terms.

- 16 VS 2925 results on PubMed for 'FastSurfer' (2020) compared to 'FreeSurfer' (2012) (silver standard)

Distribution of diseases in PubMed about 'FreeSurfer and Dementia'

- Alzheimer's disease
- Mild Cognitive Impairment
- Other
- Frontotemporal Dementia
- Parkinson's disease
- Dementia with Lewy bodies
- Primary Progressive Aphasia
- Vascular dementia
- Parkinson's disease dementia
- Subjective Cognitive Impairment
- Corticobasal Degeneration
- Huntington's disease
- Progressive Supranuclear Palsy
- Amyotrophic Lateral Sclerosis
- Posterior Cortical Atrophy
- Multiple Sclerosis
- Cerebral Amyloid Disease
- ALS-FTD spectrum
- Multiple System Atrophy

- Mild cognitive impairment: comparison difficult because of different subgroupings between studies

FIGURE 3
Pie chart showing the distribution of cohorts/diseases returned by the PubMed search "FreeSurfer and Dementia" (*n* = 428 of 493 studies, 01/01/2024).

Cohorts/diseases distribution in publications

TABLE 1 Evaluated cohorts/diseases returned by the PubMed search "FreeSurfer and Dementia" (n = 428 of 493 studies, 01/01/2024).

| Group	Found cohorts (n)	Found cohorts (%)
Sum	1,049	100.0%
Healthy / control group	356	33.9%
Alzheimer's disease	276	26.3%
Mild cognitive impairment	157	15.0%
Other	63	6.0%
Frontotemporal dementia	34	3.2%
Parkinson's disease	29	2.8%
Dementia with Lewy bodies	20	1.9%
Primary progressive aphasia*	19	1.8%
Vascular dementia	16	1.5%
Parkinson's disease dementia	12	1.1%
Subjective cognitive impairment	10	1.0%
Corticobasal degeneration	10	1.0%
Huntington's disease	10	1.0%
Progressive supranuclear palsy	8	0.8%
Amyotrophic lateral sclerosis	8	0.8%
Posterior cortical atrophy	8	0.8%
Multiple sclerosis	5	0.5%
Cerebral amyloid disease	4	0.4%
ALS-FTD spectrum	3	0.3%
Multiple system atrophy	1	0.1%

- Alzheimer's (AD) cohorts examined dominates (focus here)
- **Underrepresentation of dementias in which no specific atrophy pattern is expected**, such as vascular dementia (VD) or dementia with Lewy bodies (DLB)

Alzheimer's disease brain
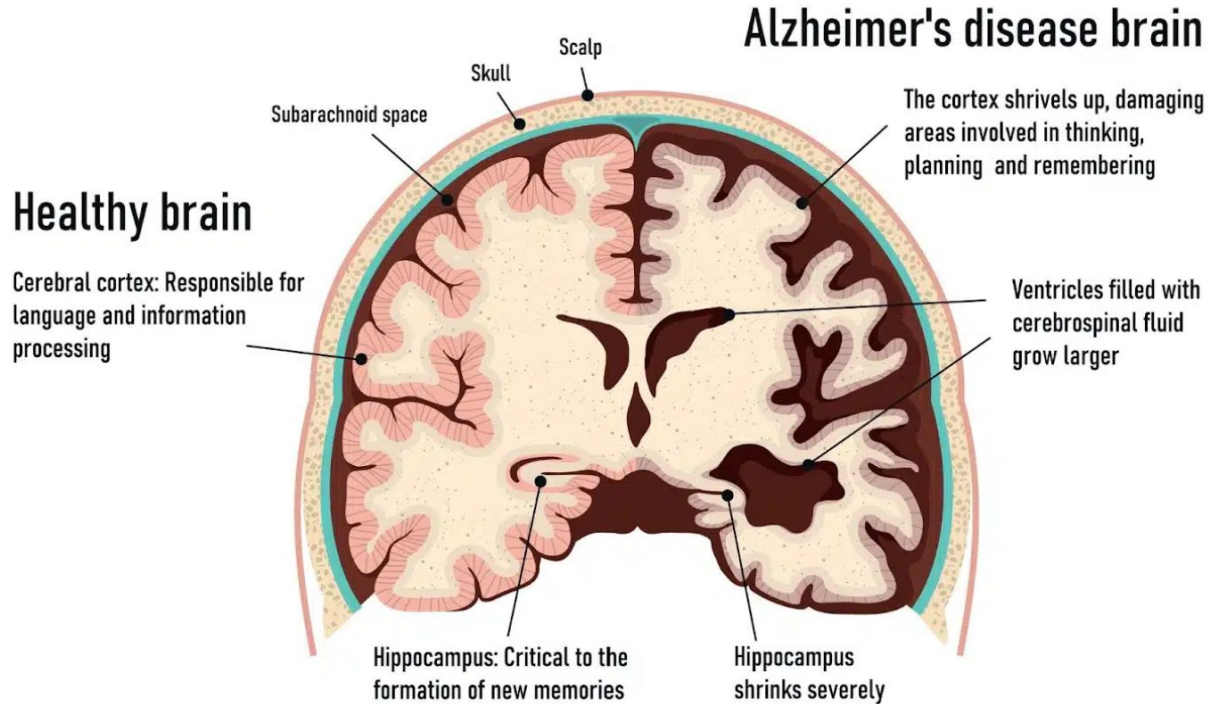
early marker of dementia (Gentreau et al., 2023)
But not completely reliable (Ferreira et al., 2017)

Used tools for "Alzheimer's disease volumetric measurement brain"
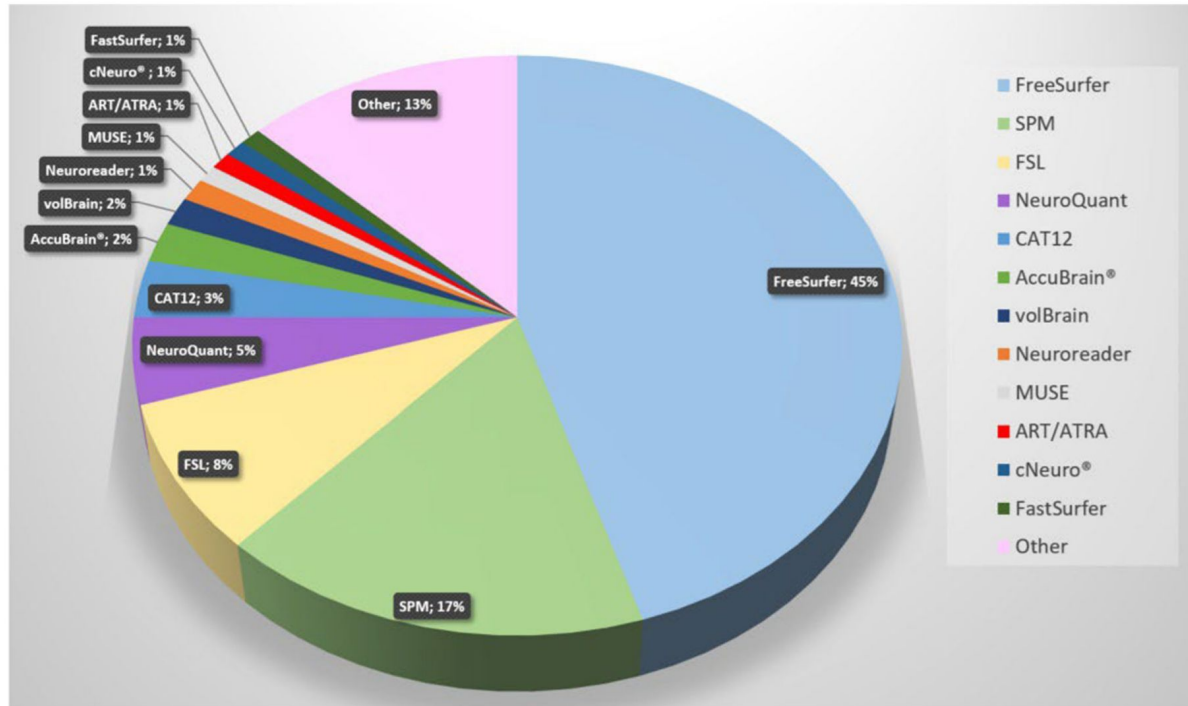
- **Statistical Parametric Mapping (SPM)**: open source, e.g. fMRI
- **NeuroQuant:** private (CA, US), cloud-based AI software, neurodegenerative diseases
- **Computational Analysis Toolbox (CAT)**: extension of SPM

- Complete list of tools and version used available in Table 2

FIGURE 4
Pie chart of software solutions in reports retrieved from Pubmed with the search term "Alzheimer's disease volumetric measurement brain" (most recent; descending). The newest 350 entries (from 2024 to 2015) were evaluated, 293 were included. All solutions with fewer than three entries are summarized under "Other".

Methods for performance assessment of the segmentation software

- **Dice similarity coefficient** (Dice, 1945; Shamir et al., 2018) (0–1, higher better)
- (Pompeiu-) **Hausdorff distance** (HD) (Birsan and Tiba, 2006) (in mm, lower better)
- **Mean average precision metric** (mAP; 0–1, higher better) (Beitzel et al., 2009)
- **Modified or Robust Hausdorff Distance** (MHD, HD95) (Huttenlocher et al., 1993) (not sensitive to local outliers)

- **FreeSurfer** is used as a Silver Standard most of the time.
- **Asymmetrical approaches needed** because of asymmetric brains (**BRATS challenge** for brain cancer segmentation, hundreds of softwares compared (Kazerooni et al., 2023), e.g. MMGan (Gao et al., 2023), nnUNetFormer (Guo et al., 2023), and multi-scale context UNet-like network (Qian et al., 2024))

Conclusion

- FreeSurfer still used as silver standard:
    - extensive functions for almost all questions and diagnosis, regular updates
    - sufficient accuracy
    - by habit (wide acceptance and validation)
    - large open source community
    - compatible with many other tools (e.g., FastSurfer, CerebNet)
- Numerous gaps in research:
    - Lewy Body Dementia sparsely researched
    - multiple atrophy patterns in Alzheimer's disease not fully understood
    - Misclassification of disease/subgrouping due to absence of biological substrate analysis (e.g. CSF biomarker profile)
    - significant variability in study protocols affects result comparability (accuracy and reliability)
- Promising new techniques:
    - **quantification in MRI using T1-and T2-mappings** (Gräfe et al., 2022; Müller et al., 2022)
    - **quantitative susceptibility mapping** (Li et al., 2024)
    - Improvement from 3 to 7-Tesla scanning (FastSurferVINN)

Thank you for your attention !