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ORIGINAL PAPER

State-of-the-Art Traditional to the Machine- and Deep-Learning-Based Skull Stripping Techniques, Models, and Algorithms

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Abstract

Several neuroimaging processing applications consider skull stripping as a crucial pre-processing step. Due to complex anatomical brain structure and intensity variations in brain magnetic resonance imaging (MRI), an appropriate skull stripping is an important part. The process of skull stripping basically deals with the removal of the skull region for clinical analysis in brain segmentation tasks, and its accuracy and efficiency are quite crucial for diagnostic purposes. It requires more accurate and detailed methods for differentiating brain regions and the skull regions and is considered as a challenging task. This paper is focused on the transition of the conventional to the machine- and deep-learning-based automated skull stripping methods for brain MRI images. It is observed in this study that deep learning approaches have outperformed conventional and machine learning techniques in many ways, but they have their limitations. It also includes the comparative analysis of the current state-of-the-art skull stripping methods, a critical discussion of some challenges, model of quantifying parameters, and future work directions.

Keywords MRI · Skull stripping · Brain extraction · Conventional skull stripping methods · Machine learning skull stripping methods · Deep learning skull stripping methods

Introduction

Magnetic resonance imaging (MRI) is considered as one of the preferred medical imaging modalities and have some advantages over X-rays and computed tomography (CT) scans, because of its non-invasive and non-ionization property. MRI has been used extensively in neuroimaging due to its capabilities of producing accurate brain scans with different contrasts like T1-weighted, T2-weighed, and FLAIR images [1] (see Fig. 1). MR images with different contrasts produce various intensity levels. MRI scans brain in different orientations, i.e., axial plane, coronal plane, and sagittal plane as shown in Fig. 2 providing high-resolution images with enhanced soft tissue contrast [1–4]. The brain MRI provides more detailed pictures as compared to other imaging modalities [5].

Brain extraction is a significant but challenging task in medical image processing [6, 7]. Brain extraction or skull stripping removes the non-cerebral tissues such as skull, dura, and scalp from brain images [8, 9]. Because of complex brain anatomy, brain segmentation cannot be solved efficiently using conventional image processing techniques. In the human body, the brain is considered as the most complex structure, so, the extraction of the brain is quite a challenging task and obtained a lot of attention because a proper diagnosis of brain disorders majorly depends upon accurate brain segmentation [10, 11]. The process of precise identification of brain regions plays a vital role in pathology, such as tissue segmentation, extraction, and multi-modality brain image registration.

Skull stripping is considered as one of the critical preprocessing step that ensures a desirable segmentation and helps in precise diagnosis of brain diseases. Skull stripping also minimizes the probability of misclassification of brain tissues during segmentation and abnormal tissues in the brain

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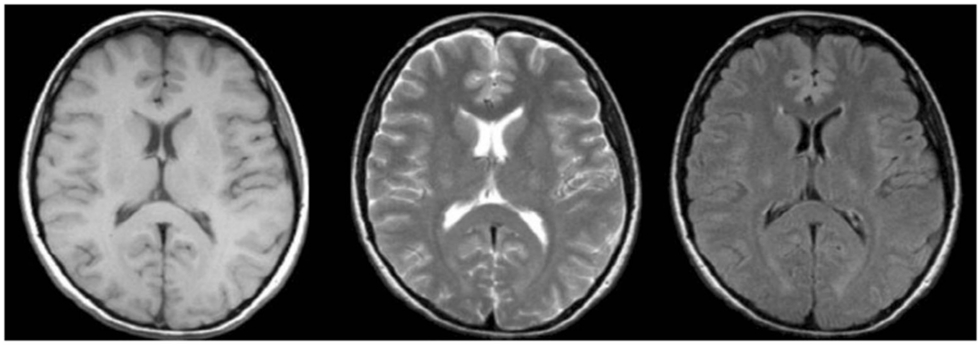


Fig. 1 Brain MRI scan with various contrasts: **a** T1-weighted image, **b** T2-weighted image, and **c** FLAIR image

[12, 13]. Accurate brain extraction enhances the possibility of auto-detection of many neuro disorders such as Parkinson's disease, dementia, and schizophrenia. The main idea of skull stripping is that it removes the non-brain tissue-like dura matter, exterior blood vessels, eyes, fats, muscles, and skull and is left only with brain region. These non-brain tissues increase the computational efficiency of various neuroimaging algorithms.

Manual brain segmentation is considered as an underlying skull stripping approach and performed by radiologists who may outline brain region manually. Still, like other manual approaches, it is prone to error and time complexity. So, the need of autotomized brain extraction methods arises. In literature, innumerable skull stripping algorithms have been defined. Many studies are being performed on the available skull stripping procedures, and their performance is analyzed on publicly available standard research datasets. It involves excluding extra-meningeal tissues from brain MR images; therefore, it is necessary to have some robust methods that classify the skull and clearly. Skull stripping techniques are classified as manual, semi-automated, and automated techniques. The particular paper provides a comprehensive review of the skull stripping methods that already exist, including conventional and some latest deep- and machine-learning-based skill stripping techniques. Figure 3 depicts the organization of the paper in detail.

The rest of the survey paper is organized as follows: the research methodology is given in "Research Methodology." "Skull Stripping Methods" is about the skull stripping methods. "Conventional Skull Stripping Methods" gives the comprehensive literature review of conventional skull stripping methods. Machine learning skull stripping methods are discussed in "Machine-Learning-Based Skull Stripping Methods." Deep learning skull stripping methods are discussed in "Deep Learning Skull Stripping." Comparative study of the conventional, machine, and deep learning methods is discussed in "Comparative Analysis of Skull Stripping Algorithms." "Model of Quantitative Analysis Measures Based on Skull Stripping Methods" is about the model of quantitative analysis measures based on skull stripping methods. "Conclusion and Future Work" draws the conclusion and future work.

Research Methodology

The methodology conducted for the survey is to find the most important and latest literature on skull stripping techniques that are based on traditional, machine, and deep learning techniques in recent years majorly from 2000 to 2019. All findings for research papers and articles have been done based on

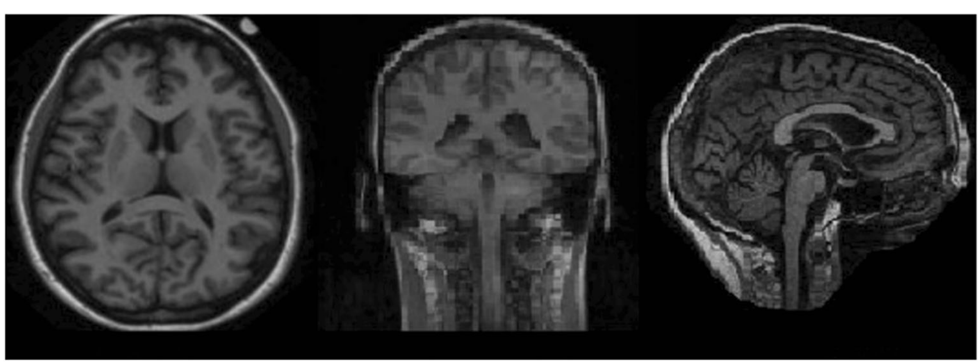


Fig. 2 MRI Brain images in multiple planes: **a** axial plane, **b** coronal plane, and **c** sagittal plane

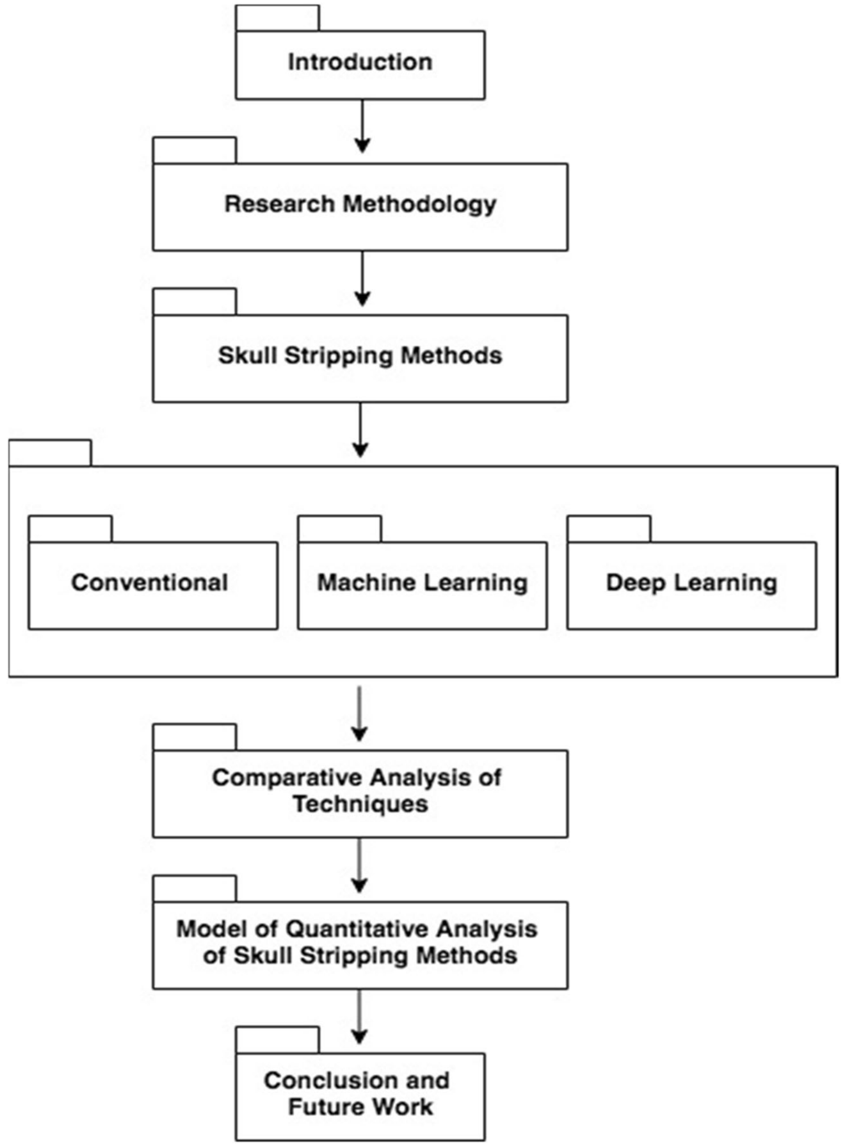


Fig. 3 It illustrates the organization of the paper based on skull stripping

IEEE, ScienceDirect, PubMed, and Google Scholar for the target years to July 2019. In this specific domain of skull stripping methods, almost 200 papers were found with the keywords: (1) skull stripping techniques, methods, and algorithms based on conventional, machine learning, and deep learning approaches; (2) different classification of skull stripping techniques; (3) MR image skull stripping; (4) brain extraction methods; and (5) skull removal.

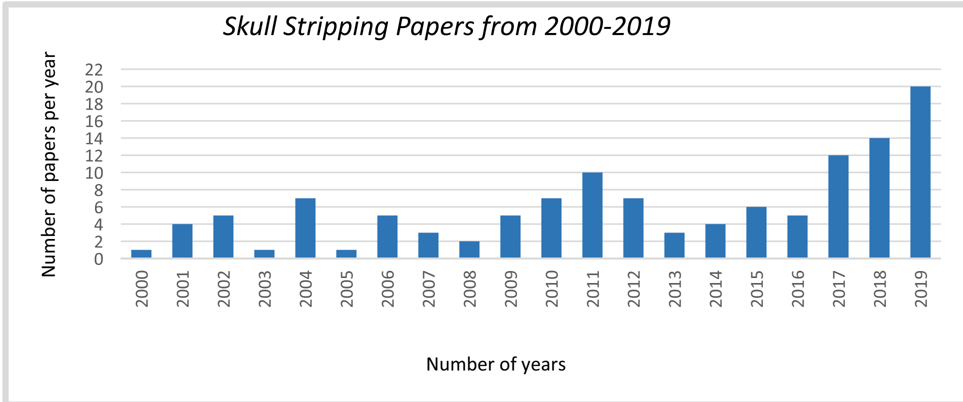
After collecting a vast literature based on the above keywords, the main task was to decide which paper to consider and which not to. For this purpose, all the abstracts, conclusions, and referred papers were studied in detail and the most relevant and important ones were made part of this survey. Skull stripping being a pre-processing step in various neuroimaging tasks, it is treated as such in much of literature where it forms part of the pre-processing section. However, this survey is focused on research papers that specifically deal with skull stripping methods.

Figure 4 shows a bar graph that indicates the number of research papers on skull stripping based on conventional, machine learning, and deep learning from the year 2000–2019. With the advancement and robustness in deep learning methods since 2016, interest in automated skull stripping around the globe has increased. For that reason, this survey has focused on the deep-learning-based skull stripping methods for the period 2016–2019.

Skull Stripping Methods

Skull stripping is classified into different categories, such as manual, semi-automated, and automated methods. This

Fig. 4 The chart illustrates the publication of articles on skull stripping based on conventional, machine-, and deep-learning-based methods included in this survey for the period 2000–2019 [1–128]



section will give a detailed discussion on numerous automated skull stripping techniques used as automated and intelligent techniques that facilitate and expedite the entire process of extracting accurate diagnostic information from brain MR volumes. In this survey, the approaches developed for skull stripping or brain MRI extraction have been divided into three major categories: (1) conventional skull stripping approaches, (2) machine-learning-based skull stripping approaches, and (3) deep-learning-based skull stripping approaches. Following Fig. 5 shows the transition of the conventional to the machine- and deep-learning-based automated skull stripping methods for brain MRI images.

The methods of conventional skull stripping are further classified into five major models. These five classes are also found in the existing literature [13] but here particularly placed under the conventional methods. (1) deformable surface–based skull stripping methods, (2) mathematical morphology–based skull stripping methods, (3) intensity-based skull stripping methods, (4) template-based skull stripping methods, and (5) hybrid based skull stripping methods. Figure 6 below describes the classification of conventional skull stripping methods into five major groups, described in detail below. It is based on the groupings generally found in the literature.

Deformable Surface–Based Skull Stripping Methods

These methods evolve and deform an active contour that fits in brain surface. They are based on the image gradient that finds the position of brain surface and is modeled by active contours. They work by defining a surface based model that iteratively deformed to fit the brain's surface of the image from its initial position until a best-fit solution is obtained [14]. In general, for brain extraction, the segmentation and performance of deformable models are better than the threshold and edge-based approaches but seem to decrease due to noise [15]. The working accuracy of these models depend upon the exact designing of the guiding forces like as geometric and statistical as well as model initialization.

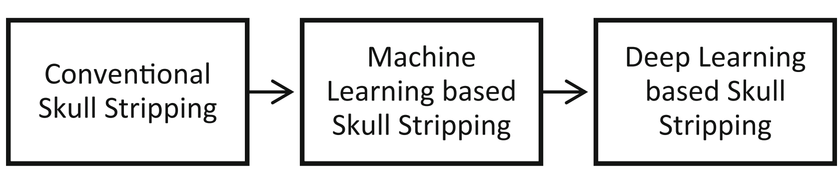
Mathematical Morphology–Based Skull Stripping Methods

Morphology-based methods are one of the automatic skull stripping techniques that work through thresholding and morphological erosion and dilation operations in series. These methods are mathematical morphological operations and edge detection based and are capable of accurate brain extraction from a normal brain MR image. At the boundary of the brain, if tumors are located, which has different intensity with normal tissues, while detecting the brain boundary, few unwanted edges appear. One of the pitfalls is that they are parameter dependent such as edge constant, diffusion iteration, diffusion, and erosion size. Such parameters are sensitive to slight changes in the data [16]. Appropriate experimentation can handle these parameters as they have a significant impact on the final results [17].

Intensity-Based Skull Stripping Methods

Intensity-based skull stripping approaches work on modeling intensity distributions of brain MR images used for threshold classification. In brain scans it separates the brain and non-brain parts by image pixel intensities. Classification based on

Fig. 5 Categorization of skull stripping methods into conventional, machine-learning, and deep-learning-based skull stripping methods



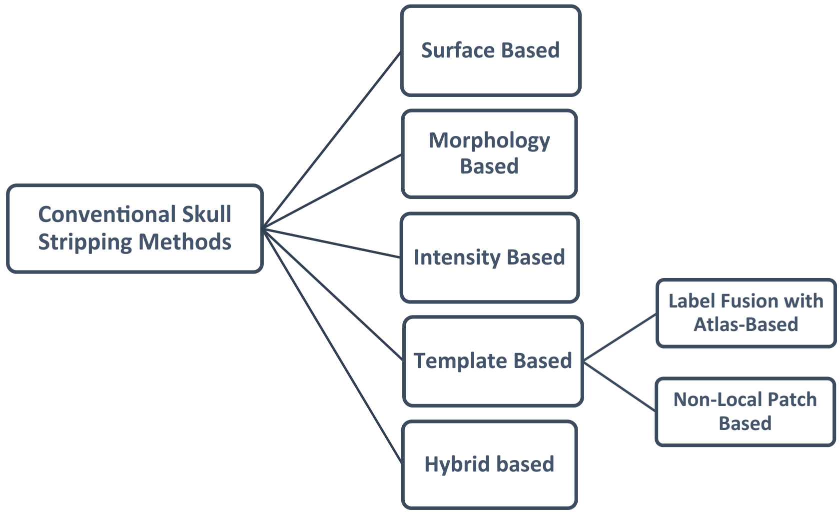


Fig. 6 The classification of conventional skull stripping methods into five major groups

intensity includes methods like histogram, edge detection, and region growing methods. These approaches are based on probabilistic models where an intensity distribution model is used for classification of the brain tissue. These techniques have the disadvantage of significant sensitivity to intensity fluctuations in brain MR images.

Template-Based Skull Stripping Methods

Template- or atlas-based approaches of skull striping rely on template or atlas on MRI of brain to separate them from non-brain tissues [18, 19]. Creating an initial approximation for the brain mask, the brain mask boundary is segmented again by a classifier, which enhances the final result accuracy. These methods vary in using number of templates to distinguish between the brain regions and also applications of these atlases. An atlas of brainis a series of section along different anatomical planes of both the healthy or diseased developing brain; a number of coordinates are assigned to every brain structure to define its outline or volume. They are robust, stable in various conditions, and have high accuracy [20]. The limitation of template-based method is the time required for construction of an atlas wherever iterative procedure is also incorporated in it [21].

Hybrid-Based Skull Stripping Methods

Hybrid, as the name implies, is the combination of more than one method from previously existing skull stripping methods.

As the conventional methods include the most frequently and popularly used skull stripping approaches. These methods generally based on the traditional image processing techniques. The above mentioned categories of skull stripping methods are mentioned and discussed in conventional techniques. Artificial intelligence (AI) is bringing a revolution in every field and especially in the medical domain. Machine and deep learning methods are of mere importance in case of automation of skull stripping techniques [7, 10]. Machine learning has a great potential for improving clinical diagnostics, prognostics, and decision-making in brain extraction and medical imaging. There are some challenges that must be considered for successful implementation. Advances in CNN deep learning architectures have contributed more for brain extraction methods. The predicted brain masks quality have been improved by using deep neural network as compared to machine learnings [7, 10]. However, from a training dataset, which consists of a collection of normal or apparently normal) brain MRI scans, such scans available commonly as compared to the brain scans with some pathological disorders, deep networks have more focus on learning image features. Thus, the performance of deep models is more sensitive to unseen pathological tissues. Figure 7 given below shows the classification and techniques of skull stripping discussed in this paper.

Conventional Skull Stripping Methods

Conventional skull stripping approaches refers to the traditional or frequently used ways of achieving skull stripping. This section includes the literature of conventional image processing methods and most frequently used skull stripping methods.

Deformable Surface–Based Skull Stripping Methods

The level set approach is a segmentation tool for images and is generally suitable for the 3D brain MR images segmentation. The level set methods have the ability to

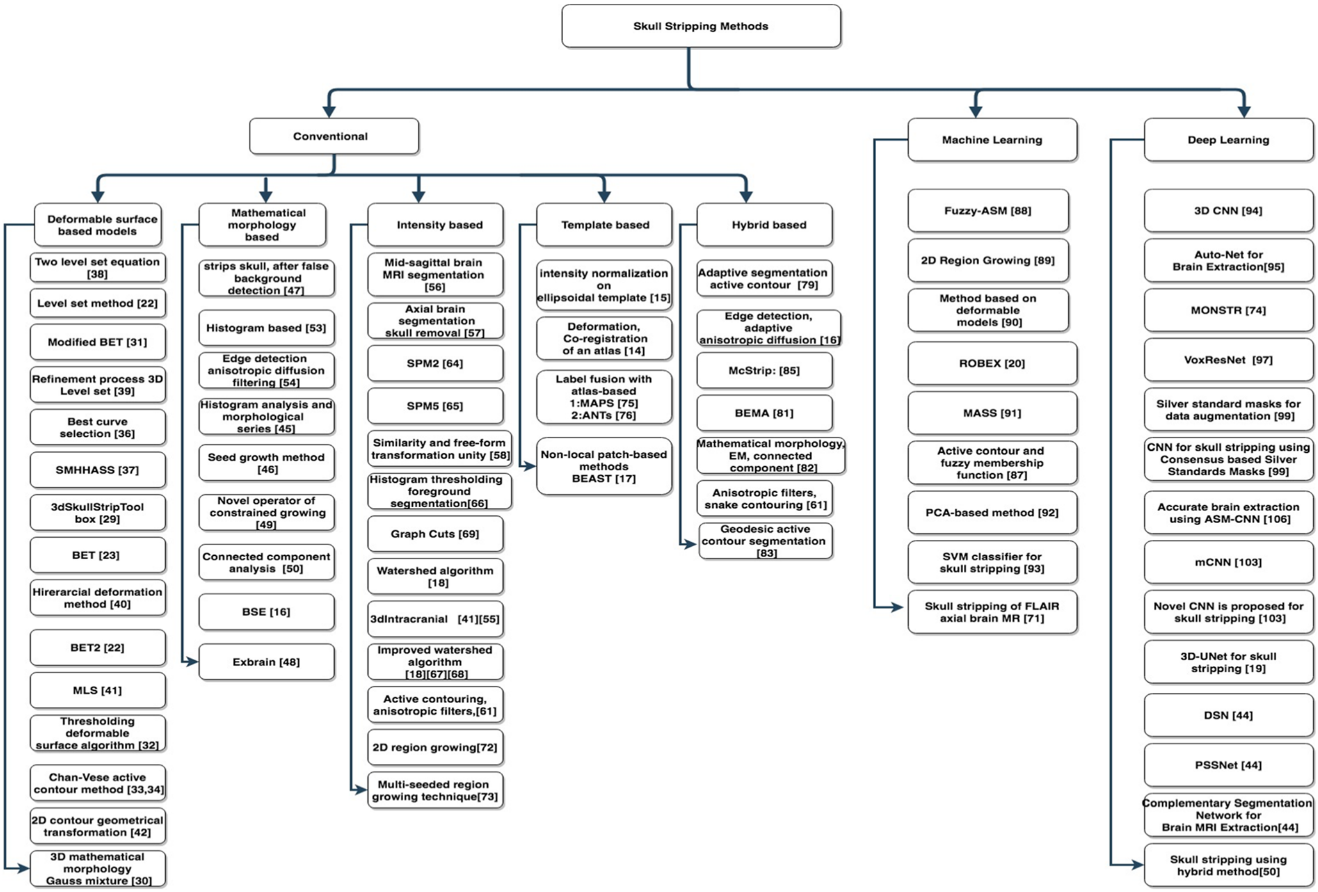


Fig. 7 Automated skull stripping method classification: conventional (deformable surface–based model, mathematical morphology, intensity, template, and hybrid based), machine-learning, and deep-learning-based methods

incorporate image-based constraints, handle complex topologies, and make the computation of geometrical properties easier like mean curvature. Baillard et al. [22] suggested a brain segmentation method from volumetric MRI using 3Dregistration and segmentation processes. It registered data of brain to a template and than from that template brain surface is used as an initial contour. Afterwards, the level set–based equation method finalizes the process of segmentation. The coupling of registration and segmentation processes enhance method quality, since the segmentation is faster, automatic, and reliable.

Brain Extraction Technique (BET), introduced by Smith et al. [23], is a deformable model approach that fits the brain surface by application of locally adaptive set models. BET is basically an intensity-based estimation of the threshold that functions to separates the non-brain and brain regions. It also establishes the head's center of gravity. On head's center of gravity basis an initial sphere is defined, and the tessellated sphere (tessellation of a surface is the tiling of a plane with one or more geometrical shapes, i.e., triangle, sphere, and hexagon, called tiles, with no overlaps, and no gaps) expands till the boundary of the brain is reached. Fractional threshold intensity and gradient are two adjustable parameters used in this method [13, 23–25]. The brain volume produced by BET is smoother than other methods but there are also chances of inclusion of some non-brain regions [26]. In the presence of brain tumor, intensity and shape variations might create problems in the evolution of the mesh, and mesh is used as the initial surface for approximating the brain surface. But, the performance of BET on such kind of images is quite well.

BET2 also proposed by Smith et al. [27] (Brain Extraction Tool v2) deformable surface model is a rapid and automated brain extracting tool that distinguishes between brain, skull, and scalp regions from MR brain images. BET2 algorithm was originally based on BET [23] to determine the brain boundary in MRI images. BET2 uses T1- and T2-weighted high-resolution images, though it can run (with less accuracy) given only a T1 [27]. It works by finding brain surface by the original BET algorithm using T1-weighted image, and subsequently, T2-weighted image is then registered to the T1 [27], using FLIRT [28].

3dSkullStrip is another skull stripping method based on the modification of BET [29] that is included in the package of

Analysis of Functional Neuro Images (AFNI). It uses T1-weighted brain MR images for skull stripping depending upon the expansion paradigm of the spherical surface. It removes eyes and the ventricles region by adopting some specific modifications.

A complete high resolution, reliable segmentation of the colored brain images and accurate skull stripping of the Chinese Visible Human (CVH) is presented by Yunjie et al. [30]. It is a model based on 3D mathematical morphology and adaptive Gaussian mixture. Brain tissue classification and bias field estimation are done by 3D mathematical morphology and Gaussian mixture model. A novel brain extraction methodology is proposed by Liu et al. [31] whose working depends upon an implicit deformable model based on the radial basis functions (RBF). They modified BET for premature infant brain segmentation using the Gaussian model and the watershed segmentation [32].

A skull stripping algorithm for brain MRI is based on Chan-Vese active contour method proposed by Somasundaram et al. [33]. This method consists of two-step fully automatic skull stripping process for proton density (PD), T1-, and T2-weighted images. Firstly, the brain is extracted from the middle slice and then in the remaining slices. In this specific method, the process for brain extraction from remaining slices was simplified by the use of adjacent slices geometric similarities [33, 34].

An idea of fast skull stripping approach is based on a refinement process and 3D level set process proposed by Hwang et al. [19]. On the tradional 3D level set methods a speedup operator is used to accelerate the evolution of level set methods. The accuracy of brain extraction methods are also improves by adopting a refinement process.

Another skull striping automation method of T1-weighted brain MR images is proposed by Zhang et al. [35] that solved the problem of boundary leakage using an enhanced geometric active contour model. When a segmented image contains some distortions at the boundaries, it leads to the boundary leakage problem. Another skull stripping approach for T1-weighted brain image is described by Somasundaram et al. [36]. The brain boundaries are identified accurately by fitting the curve that is the best among set of curves that formed at brain's boundary.

Simplex Mesh and Histogram Analysis Skull Stripping (SMHASS) is a combination of histogram analysis and deformable model–based T1-weighted MR image extraction method introduced by Galdames et al. [37]. To find an initial suitable deformation point model, a pre-segmentation step is used that depends on thresholds and morphological operations. The thresholding values are calculated by performing comparative analysis with an atlas. Table 1 comprises of the methods and limitations of deformable surface–based skull stripping methods.

Mathematical Morphological Operation–Based Skull Stripping Methods

A three-step procedure of skull stripping utilizing morphological processing, anisotropic diffusion filtering, and edge detection proposed by Gao and Xie [43] and the results show that it can segment brain precisely. Anisotropic diffusion reduces image noise without the removal of significant image parts, typically edges or other details Sometimes mathematical morphological methods are sensitive to minor variations in data and create problems in finding the suitable morphology for brain tissue separation [15, 44]. A much similar algorithm proposed by Tsai et al. [45] is based on morphological operations and analysis of histogram.

Another method for segmenting brain MR images automatically is a seed growth and threshold-based [46]. In this method seed growth and threshold techniques are used to classify brain tissues from T1-weighted MR images. This is a simple mathematical algorithm as only manipulations based on intensity and for particular intensity scanning values are involved and the seed values are chosen automatically.

For the removal of skull, Sajjad Mohsin et.al [47] implemented a mathematical morphological algorithm after false background detection. The drawback of this algorithm is that it fails on noisy and low-contrast images by analyzing intracranial volumes as the brain cortex extraction from T1-weighted images.

Brain surface extraction (BSE) lies in the category of mathematical morphological–based methods for skull stripping from T1- and T2 weighted images developed by Shattuck [16], and it works on morphological operators and edge detectors to strip the skull. It employs anisotropic diffusion filtering and a 2D Marr Hildreth edge detector for anatomic boundary identification. BSE disconnects brain and non-brain tissues using morphological erosion operation, and largest connected component (LCC) is extracted as the brain. To undo the erosion effect a corresponding dilation operation is applied. At last, a morphological closing operation is applied by BSE that fills minute holes that may exist in brain surface and the tissues of non-brain is still connected to the brain are removed. BSE is edge detecting–based algorithm, sometimes with poor contrast images it may fail to work.

Brain extraction algorithms (BEAs) for processing take T1-weighted image as due to high resolution, they are considered as the gold standard in terms of morphological or anatomical neuroimaging [48–50]. In the case of brain pathology, T2-weighted images are quite sensitive [51].BEA [52] segments brain using diffusion, morphological operations, and connected component technique for brain extraction in T2-weighted images. BEA for T2-weighted images, low-pass filter (LPF) is applied for background noise removal. After that, the brain boundaries are enhanced by diffusion and a threshold intensity value is obtained for binary brain image. The method is named

Table 1 Different method, MR modalities, and their limitations of deformable surface–based skull stripping methods

Methodology	Issues	MR modality
Two level set equations [38]	Greater computational time	T1-weighted image
Level sets methods [22]	Greater computational time and utilizes complex level set	
Modified BET, Gaussian model, and watershed segmentation [31]	For result accuracy T2-weighted images are required	
Refinement process and 3D level set [39]	Requires exact speedup operator calculation for curve refinement	
Improved geometric active contour [35]	Accurate calculation of speedup operator for curve refinement	
Best curve selection [36]	Complex computation	
SMHASS [37]	Complex thresholding	
3dSkullStrip Tool box [29]	Parameters adjustment required	
BET [23]	In bottom axial slices unable to extract the brain region	
Hierarchical deformation model [40]	Initialization of model is complex	
BET2 [22]	Input images are T1 and T2	T1- and T2-weighted images
MLS [41]	Unable to perform well on images with noise and poor contrast	
Thresholding, deformable surface–based algorithm [32]	Image contrast effects the results	
Chan-Vase; active contour model [33, 34]	Complex computation	PD, T1-, and T2-weighted images
2D contour geometrical transformation [42]	Perform well on normal brain images	3D T1-weighted image
3D mathematical morphology and Gauss mixture [30]	Intensity bias affects the output	

as 2D-BEA as it only uses 2D information from a single slice. The problem with 2D-BEA is that LCC is unable to perform well in a few slices. To overcome drawbacks of 2D-BEA, 3D-BEA came into existence that uses the 3D information available in adjacent slices. Below given Table 2 describes the mathematical morphological–based skull stripping methods.

Intensity-Based Skull Stripping Methods

An automatic 3dIntracranial method is intracranial part segmentation in both T1- and T2-weighted brain MR images [41, 55]. The model works by computing a down hill simplex method computing standard deviations, means, and weights of presumed background, gray matter (GM), and white matter (WM). In brain WM is buried deep and GM is found on the brain's surface, or cortex. T1-weighted images provide contrasts between GM and WM as dark gray and lighter gray, respectively. Whereas, T2-weighted images demonstrate contrast between GM as light gray and WM as dark gray.

A probability density function (PDF) is computed which set boundaries of high and low signal intensity from the above estimated values, and non-brain voxels are excluded from these boundaries. Slice-by-slice application of connected component analysis is used to demarcate the brain. A neighborhood analysis is carried out finally at every voxel to either exclude or include the misclassified ones. Nine parameters are required in this technique for each image estimation and improper estimation, and initialization leads to the poor results [15]. Another segmentation algorithm for 3D sagittal brain MRI was developed by Huh [56] based on the connectivity threshold to extract brain from 3D sagittal MR.

Suzuki and Toriwaki proposed an automatic skull stripping method [57] in axial MR slices that separates brain tissues from others. Initially, thresholds are adjusted, and the brain region iteratively fits in, based on the resulting masks' geometry. It shows limitation in RF inhomogeneity presence and in slices where brain region is inhomogeneous. A method of skull stripping that is a 3D segmentation of internal brain structures is developed by Dawant et al. [58] using similarity and free-form transformation [59, 60].

Another automated brain segmentation method was proposed by Stella and Blair et al. [61, 64]. This method is based on active contouring, anisotropic filters and brain anatomy information. By using the above-mentioned techniques eyes like complicated structures can be removed quite easily from the brain MRI. It is a multistage procedure that involves background extraction, and a rough outline of brain is traced and converted to a final mask [36, 62, 63].

Table 2 Different method, MR modalities, and their limitations of mathematical morphological–based skull stripping methods

Methodology	Issues	MR modality
Mathematical morphological algorithm It strips skull, after false background detection [47]	Fails on noisy and low-contrast images by analyzing intracranial volumes	T1-weighted images
Thresholding and morphological operations based on histogram [53]	Find difficulty to locate the ideal morphology size for discriminating brain tissues	
Morphological processing, edge detection and anisotropic diffusion filtering [54]	Unable to identify blood vessels completely from brain due to noise and leads to incorrect identification of brain boundary	
Histogram analysis and morphological operations series [45]	With numerous image artifacts skull stripping result are not effective.	
Seed growth, threshold-based method [46]	Estimation of threshold must be accurate	
Edge detection thresholding, connectivity, and a novel operator of constrained growing [49]	Brain segmentation may be affected by intensity bias	
Connected component analysis and morphological operations [50]	Under/over segmentation in results of intensity inhomogeneity images	
BSE [16]	Dura matter presence in brain mask, Marr–Hildreth edge detector is unable to identify a clear brain boundary	T1- and T2-weighted images
Exbrain [48]	The initial threshold value effects the segmentation performance	3D T1-weighted images

Voxel-based morphometry (VBM) using statistical parametric mapping (SPM2) is another automated method for assessing atrophic statistical differences between various groups of subjects in brain MRI [64]. Brain mask is not completely generated by SPM2 [64] but obtains from the sum of WM and GM regions after brain segmentation in T1-weighted brain MR images. SPM2 [64] is updated to SPM5 [65]. Unlike SPM2, a probabilistic brain tissue segmentation method is used by SPM5. It is a combination of tissue classification, bias correction, and image registration.

A skull stripping algorithm Histogram-based BRain Segmentation (HBRS) is proposed by Zu et al. [36, 66] based on thresholding, morphological operations, histogram analysis, and foreground/background segmentation of T1-weighted images. It is an accurate, simple automated algorithm for segmenting 3D brain and volume measurement in T1-weighted brain MR images. This algorithm consists of three steps, i.e., foreground/background thresholding, removal of skull, and residue fragments (sinus, CerebroSpinal Fluid (CSF), dura) [66].

Hahn and Peitgen [18] proposed a completely intensity-based watershed algorithm using a simple merging criterion to avoid the over segmentation depending upo a single parameter. The proposed method is particularly suitable to segment brain and robust to intensity inhomogeneities. Sometimes, it is unable to remove dura and skull [67].

An updated watershed algorithm is proposed by Grau et al. [18, 67, 68] to segment WM/GM in brain MR images. Instead of calculating gradient, different prior information based difference functions for various applications are used by this method. For the segmentation of WM/GM, these functions are calculated from the probability values for every voxel and class.

Sadananthan et al. [68, 69] propose the skull stripping approach named as graph cuts for T1-weighted images, it is an appropriate intensity threshold that lies between the mean intensities of CSF and GM. For the removal of narrow connections removal graph cut is used that works on the basis of graph-theoretic image segmentation approach to locate the cuts for dura removal, instead of using morphological operations. Some drawbacks of this method are trivial brain loss in case of a few datasets, but for the practical application, it can be neglected. Due to less preservation of dura, segmentation can create some problems [69].

A very simple method of 2D region growing method for skull exclusion was proposed by Somasundaram and Kalavathi [70, 71]. Another method includes segmentation of brain using method of multi-seeded region growing [75]. In order to extract brain from PD, T1-weighted, and T2-weighted images for all orientations coronal, axial, and sagittal brain MR images multiple seed points are used. Following Table 3 describes the intensity-based skull stripping methods.

Template-Based Skull Stripping Methods

Skull stripping technique is a preprocessing step for reconstructing cortical surface proposed by Dale et al. [15]. Wang et al. [14] give a method that initially strips skull by co-registration of an atlas, followed by a refinement process with

Table 3 Different method, MR modalities, and their limitations of intensity-based skull stripping methods

Methodology	Issues	MR image modality
Mid-sagittal brain MRI segmentation utilizing connectivity-based threshold, landmarks, and anatomical information, [56]	Noise, intensity inhomogeneity, and image artifacts may affect the results	3D sagittal brain MRI
Axial brain MRI tissue segmentationusing using iterative thresholding [57]	Shows limitation in RF inhomogeneity presence and in the brain inhomogeneous slices	3D axial MR slice
SPM2: Tissue segmentation using GM and WM [64]	Poor at removing non-brain tissues accurately	T1-weighted images
SPM5: Image registration, tissue segmentation, and bias correction [65]	Initial parameters are hard to find	
Similarity and free-form transformation unity [58]	Not applicable to pathological brain image	
Histogram analysis, thresholding, and segmentation of foreground/background [66]	Brain segmentation is not accurate due to morphological operations.	
Graph Cuts [69]	Brain loss for some data sets	
Watershed algorithm [18]	Noise sensitive and over-segmentation	
3dIntracranial [41, 55]	Nine parameters are required and inaccurate initialization and estimation leads to improper brain segmentation	
Improved watershed algorithm	Markers affects the brain segmentation	T1- and T2-weighted images
Combination of the watershed algorithm and atlas registration [18, 67, 68]		
Active contouring, anisotropic filters, and prior knowledge of brain anatomy [61]	Multistage process	
2D region growing [72]	Inaccurate results with large intensity bias	PD, T1-, and T2-weighted MRI
Multi-seeded region growing technique [73]	Unable to perform on brain images with large intensity bias	

a scheme of deformation surface guided by the prior information.

Non-local Patch–Based Methods

Non-local patch methods are successfully used in various applications of neuroimaging, such as tissue segmentation, classification, lesion segmentation, registration, super resolution, intensity-based normalization, and image synthesis [20]. These methods include brain extraction using non-local segmentation technique, Multi-cONtrast brain STRipping (MONSTR) [74]. They achieved remarkable performance of accuracy and robustness [20]. Brain Extraction based on non local Segmentation Technique (BEaST) proposed by Eskildsen et al. [17] is a method of skull stripping that depends on non-local segmentation process.

Label Fusion with Atlas-Based Techniques

Label fusion with atlas-based techniques, such as Multi-Atlas Propagation and Segmentation (MAPS) [75], Advanced Normalization Tools (ANTs) [76], and Pincram [77], use deformable model implement registration of multiple atlases to a target subject. In the target space after being registered, brain masks in all the atlases are combined together by using Simultaneous Truth and Performance Level Estimation (STAPLE). In these approaches, the main operation is the registration process, so, their performance depends upon registration accuracy and brain mask quality in each atlas. Following Table 4 describes the methods and limitations of template-based skull stripping methods.

Hybrid Method–Based Skull Stripping Methods

T. Kapur et al. [78, 79] introduced a hybrid technique based on three existing operations that are adaptive segmentation [80], active contour, and morphological operations. Shattuck et al. [16] use edge detection, morphological erosions, and adaptive anisotropic diffusion erosions to locate brain.

To get rid of some of the limitations of individually existing techniques, Rex et al. [81] proposed an algorithm named Brain Extraction Meta-Algorithm (BEMA) that combines results of various algorithms of skull stripping algorithms including BET [23], BSE [16], 3dintracranial [41], and watershed algorithm [15] for T1-weighted images. Another hybrid method that is a combination of connected component analysis, Expectation Maximization (EM) algorithm, and mathematical morphology with some pre-processing and post-processing techniques and geodesic active contours to segment the brain proposed by Huang et al. [82]. Bauer et al. [83] proposed another hybrid skull stripping method for T1, T2-weighted, FLAIR images, and CT scans. The algorithm

Table 4 Different methods, MR modalities, and limitations of template-based skull stripping methods

Methods	Issues	MR image modality
Deformation process and intensity normalization on ellipsoidal template [15]	Computationally heavy	T1-weighted images
Deformation scheme and co-registration of an atlas [14]	Refinement and manual extraction of atlas	
(a) Label fusion with atlas-based techniques		
Methods	**Issues**	**MR image modality**
MAPS [75]	Accuracy of segmentation based on the best fitted atlas	T1-weighted images
ANTs [76]	Multiple threading strategies	
(b) Non-local patch–based methods		
Methods	**Issues**	**MR image modality**
BEAST [17]	Underestimates the brain masks by removing lesions	T1-weighted images

uses template-based geodesic active contour segmentation with MLS algorithm and implemented in ITK.

A fully automated brain segmentation algorithm was proposed by Atkins and Mackiewich [61, 68]. This hybrid model uses snake contouring and anisotropic filters, which remove the eye region in brain MR images. This method works for axially acquired multi-spectral datasets T2-weighted brain MR images [84] and was modified for coronal T1 datasets [48].

Minneapolis consensus Stripping (McStrip) is proposed by Rehm et al. [70, 85], a hybrid algorithm for T1-weighted brain MR images implemented in Interactive Data Language (IDL) using BSE [16]. It depends upon template based extraction through non linear warping, intensity thresholding with connectivity constraints, and edge detection with morphological operations. McStrip is initialized with a mask using Automated Image Registration (AIR) [85] and coarse mask is formed by the dilation of AIR mask. Thresholding values for both brain and non-brain tissues are estimated by coarse mask, and threshold is set automatically to generate a mask. After void filling and smoothing a final McStrip mask is created by combining threshold and BSE masks [70]. The given below Table 5 discusses the methods and limitations of hybrid-based skull stripping methods.

Machine-Learning-Based Skull Stripping Methods

The literature of skull stripping in machine learning domain is discussed in this section. Brain and non-brain tissue segmentation in MR images require reasonably high accuracy and speed. While traditional skull stripping techniques require adjustment of several numerical parameters depending on the dataset to achieve reasonable results, whereas machine-learning-based skull stripping techniques are developing to achieve more effective results.

Model-Based Level Set (MLS) method [86] is used for the skull and intracranial tissues removal that are surrounded by the brain in both weighted images, i.e., T1- and T2-weighted MR images. MLS depends on the intensity difference of different brain parts and curvatures of the brain surfaces.

For WM/GM segmentation in brain MR slices region based level set snakes are quite a powerful approach. Suri et al. [88] proposed a region based level set snakes WM/GM in brain MR images. A fuzzy membership function is used for classifying images into the background, GM, WM, and CSF. Then active contour is evolved by a deformable model and a gradient detector that fits the surface between the GM and CSF.

Kobashi et.al [68, 88] proposed Automated Fuzzy logic-based Skull Stripping (AFSS), a method for infant's MR brain skull stripping. AFSS is used to estimate the intensity distributions by the use of a priori knowledge based upon the Bayesian classification with Gaussian mixture model. The prior knowledge is described by fuzzy membership functions, using estimated intensity distribution; fuzzy rule–based ASM segments the outer brain boundary. It is an unsupervised learning-based approach.

An automatic method of skull stripping for T1-weighted images depends upon statistical shape model proposed by Lao et al. [40]. The particular proposed surface-based model is hierarchically represented by overlapping sets of surface patches, each patch has few elastic properties, and the training set learns the range of deformation surface. This hierarchical model of deformation increases the robustness to local minima. The model is deformed to brain's outline by process of matching local image and similarity evaluation in the whole patch. The results shows an high agreement between supervised and automatic skull-stripping methods.

A clustering and 2D region growing skull stripping method for brain MR images is proposed by Somasundaram et al. [89]. To identify brain boundary inside the skull, a clustering-based technique is used. The cluster centroids are found and connected to form the brain boundary. All the

Table 5 Different methods, MR modalities, and their limitations of hybrid methods for skull stripping

Methodology	Issues	MR image modality
Adaptive segmentation, active contour, and morphological operations for brain segmentation [79]	Brain segmentation is inaccurate	T1-weighted image
Edge detection, adaptive anisotropic diffusion, and morphological erosions [16]	Partial volume tissue measurement	
McStrip: Nonlinear template warping, intensity-based thresholding with connectivity constraints, and edge detection, Incorporates BSE [85]	Accurate wrap masks are required from different models using automated image registration	
BEMA, BSE, BET, 3dintracranial, and watershed algorithm [81]	Computationally heavy limitations of every method also effect the performance of BEMA	
Mathematical morphology, expectation maximization (EM) algorithm, connected component analysis, pre-post processing techniques, and 3D geodesic active contours [82]	Segmentation based on pixel intensity	
Anisotropic filters and snake contouring technique [61]	Manual initialization is required for few slices in snake contouring model	T2-weighted images
Geodesic active contour segmentation using ITK [83]	Manual tuning of parameters using registration and level set segmentation	CT images, T1, T1-contrast, T2, T2-flair Weighted Image

clusters are connected using 2D region growing method. By the same region growing method removal of the skull and clusters outside the skull is achieved.

For segmenting brain region, a new method is developed based upon deformable models [90]. This specific method attempts to find the solution of the segmentation method using deformable organisms to create an easily customizable segmentation plan. If the data are noisy in certain areas, this method works without affecting the final segmentation.

ROBEX [20] is a RObust, learning-based Brain EXtraction system. In the skull stripping context, it is considered as the first hybrid generative/discriminative model. The discriminative model functions as a random forest classifier and trained to identify the boundary of brain , whereas generative model is described as a point distribution model ensuring the acceptance of results. Whenever a system is introduced with a new image, the generative model starts exploring it and finds the highest likelihood contour in accordance with the discriminative model [20].

Multi-Atlas Skull-Stripping (MASS) presented by Doshi et al. [91] is an automatic brain extraction of brain MR images, based on a multi-atlas registration framework. It provides a unique framework of three-part template selection, registration, and label fusion for obtaining accurate results. This method adopts a strategy of specific template selection that fits the best of anatomical variations within the data set.

Miranda et al. [21] introduced a slightly different work on skull stripping, i.e., the improvement in center of gravity (COG) estimation of the brain MR images using 3D Haar-like features. According to this study better estimation of the pose will advance the results of posterior skull stripping of the BET. It is validated on both T1- and T2-weighted images of the brain MR and also considers as the first study to analyze the impact of COG estimation over skull-stripping of brain MR images.

For brain extraction, a specific PCA-based model is designed from pathological images. Brain MR image is decomposed into three parts in this method. Sparse term captures the non-brain tissue outside of the normal brain tissue that is reconstructed as a quasi-normal image close to a normal PCA space, and a total-variation term is used to capture brain pathologies [92].

SVM has been used as a classifier for skull stripping in T1-weighted MR images as proposed by Sjolund et al. [93]. The method gives a very precise segmentation as compared to both mathematical morphological and a deformable surface method. Global and local information is used as input, and the latter is required to differentiate between air and bone as depending only on the local image intensity it is not possible [93].

Another machine learning skull stripping approach of FLAIR axial brain MR scans was presented by Jerry Li et al. [112]. This method predicts each pixel as part of brain tissue or not using either classification or clustering estimators.

Table 6 gives a very quick overview of the machine-learning-based skull stripping methods.

Deep Learning Skull Stripping

This section gives the literature review of the latest deep learning skull stripping approaches. Recently, the latest use

Table 6 Different machine learning methods for skull stripping

Methodology	MR modality	Learning approach
Fuzzy-ASM [88]	Not specified	Unsupervised
clustering and 2D region growing [89] Method based on deformable models [90]	T1-weighted image	Supervised
ROBEX [20]		
generative/discriminative		
MASS [91]		
Active contour and fuzzy membership function [87]		
PCA-based method [92]		
SVM classifier for skull stripping [93]		
Skull stripping of FLAIR axial brain MR [71]	FLAIR	Supervised

of deep learning approaches in skull stripping suggests that it is an active research field [94, 95]. Deep learning is carried out by a convolutional neural network, with parameter and hidden layers. In deep learning unlike normal neural network, each input of MR image passes through a convolution layers series.

Deep-learning-based segmentation is usually done using two main approaches: (1) a voxel-wise network uses CNN architectures with FC layers for classifying the central pixel in an image patch and (2) a fully convolutional network (FCN) [96] segments the whole image at one feed forward step.

Kleesiek's method is considered as the base of the state of the art skull stripping methods in deep learning since 2016. They proposed a voxel wise 3D CNN. [96]. It is a supervised learning approach that gives state-of-the-art performance as compared to other existing conventional techniques for skull stripping. For brain segmentation, VoxResNet approach is used that is based on ResNet-based architecture [97]. Kamnitsas et al. [98] proposed an efficient multi-scale 3D CNN with fully connected conditional random fields (CRFs) for segmentation of brain lesion.

Consensus methods are being used increasingly in medical problems. These methods provide more accurate and reliable segmentation labeling in skull stripping and other tasks of image processing. Such methods generate annotated data from different automatic methods. Rex et al. [81] give the comparison of proposed consensus methods with other automatic methods, and the results are improved than different segmentation done by experts [82]. Silver standard masks for data augmentation can also be generated by consensus masks [81]. A dataset named CC-359 released by Souza et al. [99] containing silver standard masks is generated by Simultaneous Truth and Performance Level Estimation (STAPLE), which is a consensus algorithm. It is the first effort to analyze the influences of both magnetic field strength, scanner, and vendor on skull stripping.

Lucena et al. [99, 100] for data augmentation in deep-learning-based skull-stripping introduces the use of silver standard masks. These masks are formed by the use of consensus algorithm STAPLE and are compared to gold standard generated models and have improved generalizability due to the consensus method. At the training stage, silver standard masks augment the input dataset minimizing the manual segmentation at this step. A robust CNN method of skull stripping, proposed by Lucena et al. [99], uses fully trained silver-standard mask [100]. The particular proposed method analysis indicates that their auto-context CONSNets are comparable to the latest automated approaches. This method is considered as the first truly big data one for skull striping methods [100].

Another skull stripping method named as a sparse patch–based Multi-cONtrast brain STRipping method (MONSTR) is proposed by Roy et al. [74]. It is an atlas-based approach where non-local patch information from more than one atlas contains multiple MR sequences and reference delineations of brain masks are joined to produce a targeted brain mask. One of the advantages of MONSTR is that it uses multiple MR sequences, i.e., T1, T2, and other imaging modalities like CT scans. MONSTER outperforms the brain extraction task when compared with BEaST, SPECTRE, OptiBET, and ROBEX.

Salehi et al. [84] proposed auto-context CNN brain extraction method. Two parallel approaches 2D FCN U-Net and parallel voxel-wise networks followed by an auto-context CNN classifier were inspected in auto-net method [100]. Auto-context CNN classifier works by concatenating the probability maps and then they are used as an input data to another CNN followed by the auto-context algorithm [101]. This proposed methodology aims to design an accurate, geometry-independent, registration-free, and learning-based brain extraction. The auto-context CNNs, i.e., Auto-Nets: 2.5D and U-net, outperformed over an approach of deep learning and conventionally used brain extraction approaches 3dSkull, HWA, BET and Robex.

Duy et al. [102] proposed a fusion of Active Shape Model (ASM) and CNN-based skull stripping method, and they collectively named them as Active Shape Model and Convolutional Neural Networks (ASM-CNN). The method works on 2D image sequences in sagittal plane instead of whole 3D structures. At first, to estimate the brain region an improved version of ASM is used with optimal features and the brain boundary is refined by a CNN constructed and trained. Finally, CRF and Gaussian processes are used for the post-processing of the brain region. The ASM-CNN approach can produce accurate segmentation in all cases, even with the small and dispersed brain regions.

An algorithm named Multistable Cellular Neural Network (mCNN) for skull stripping is proposed by Yilmaz [103]. It has the ability to perform on both T1- and T2-weighted brain MR images. mCNN uses cellular neural networks (CNNs) and multistable CNN structures along with contrast enhancement and noise reduction algorithm.

Dey et al. [104] proposed Complementary Segmentation Networks (CompNets) for accurate brain extraction of both pathological and normal brain from T1-weighted images. This study investigates multiple complementary CompNets. Generally, CompNets architecture has two paths: one is learning of brain tissues and generation of brain masks and the other step learns brain's outside environment and generates an approximate brain mask. There are three existing types of CompNets, i.e., the plain, the probability, and the optimal CompNets. This novel CompNet increase the roubustness of segmentation by incorporation of the object of interest learning process [83]. Five different types of techniques are compared qualitatively, i.e., plain U-Net, dense U-Nets, probability, plain, and optimal CompNets on both the normal and pathological disorder brain scans. Optimal CompNets outperforms for both the normal or pathological images among all the other networks.

CNN is proposed for segmenting brain region by Selvathi [104]. They remove the noise first from MR images using Non-Local Mean (NLM) filter, and the skull portions are removed by using CNN. Kebir et al. [105], proposed a hybrid technique based on FCM, GMM and active contour to identify brain regions in MR scan. The skull stripping is evaluated, and the results indicate that the proposed method outclasses the most popularly used skull stripping algorithms, i.e., BET, BSE, ROBEX, and ASM-CNN. Hwang et al. [19] proposed usage of 3D-UNet for skull stripping, that is an end-to-end deep learning segmentation approach. It is a fully automatic skull stripping method and is widely used for volumetric segmentation. Its results are successful in real brain MRI datasets.

Deep segmentation network (DSN) proposed by Sikka, et al. [44] is a supervised deep-learning-based approach for extraction of brain. It is capable of learning many anatomical features of the brain MR scan automatically even on the training of smaller dataset. The method has been performed using T1-weighted MR image, but the training can be done using T2-weighted image or PD modality making it more versatile across multiple modalities.

A supervised automatic neonatal skull stripping method is named as multi-view Pyramid Skull Stripping Network (PSSNet) proposed by Gao et at. [44]. This method is a modification of pyramid scene parsing network [44] and robust on neonatal T1-weighted MR images and feasible in clinical applications. A deep learning pipeline (DLP) with a triple network framework is proposed by Yogananda et at. [54] using T1-weighted image performs skull stripping and brain segmentation into CSF, GM, and WM. Table 7 comprises of various deep-learning-based skull stripping methods.

Comparative Analysis of Skull Stripping Algorithms

This section will discuss a brief comparison of conventional, machine-learning, and deep-learning-based skull stripping methods. A comparative analysis of four brain extraction tools, i.e., McStrip [85], SPM2 [85], BET [23], and BSE [16] using T1-weighted MR brain images given by Boesen et al. [107], is discussed with respect to their performance. According to the analysis [107] McStrip, a hybrid algorithm outperformed SPM2, BET, and BSE; however, on processing time BET and BSE outperformed McStrip. Another comparative study on skull stripping methods, conducted by Fennema et al. [108], compares BET [23], 3dIntracranial [41], HWA [69], and BSE [38] to find effects of bias correction, image type, and local anatomy of brain slice. According to this study HWA [78] removes substantial non-brain tissues from the complicated regions of face and neck while retaining the area of brain. BSE reaches the brain boundary and rarely also removes some brain tissue. 3dIntracranial and BET sometimes leave non-brain regions behind and removes the brain region. BET [23] and BSE [16] are compared in a study [108], and both methods produce under and over-segmentation, and also, these methods are not completely insensitive to subject characteristics. MONSTR [74] when compared with other stripping algorithms BEaST, SPECTER, OptiBET, and ROBEX produces more precise results on both the healthy and with pathological cases such as TBI and tumor [106]. The performance of PCA-based skull stripping methods [92] are compared with popularly used brain extracting methods, i.e., ROBEX, BEaST, MASS, BET, BSE, and the Kleesiek's method. PCA-based skull stripping method performs better than these competing methods on IBSR, LPBA40, and the TBI datasets.

Auto-context CNN that outperformed the Kelsie's method, accurate and reliable automated brain extraction BET, 3dSkullStrip, ROBEX, and HWA. ANTS, STAPLE, and BEaST achieve the highest dice coefficients [99], which is a compromise between specificity and sensitivity, but they are not robust as BEaST, ANTs, and MBWSS achieve comparable results and segments the brain fissures accurately. ASM-CNN [106] has remarkable dice coefficients and Jaccard indexes when tested on IBSR, LPBA, and OASIS datasets in both 2D and 3D structures and performed well on BET, BSE, 3DSS, BEAST, and ROBEX. CompNets [109] compared, and with Kleesiek's method, a plain and a dense U-Net and

Table 7 State of the art deep learning skull stripping methods

Methodology	MR modality	Dataset used	Learning approach
3D CNN [94]	T1-weighted,T2-weighted, and FLAIR images	IBSR LPBA40 and OASIS	Supervised
Auto-Net for Brain Extraction [95]		LPBA40 and OASIS	
MONSTR [74]		ADNI, MRBrainS, and NAMIC	
VoxResNet For brain extraction [97]	T1-weighted, T2-weighted, and FLAIR images	Private Dataset	Supervised
Silver standard masks for data augmentation [99]	T1-weighted images	LPBA40, CC-359, OASIS	Supervised
CNN for skull stripping using Consensus-based Silver Standards Masks [99]		CC-359, LPBA40, and OASIS	
Accurate brain extraction using ASM-CNN [106]		IBSR, LPBA, and OASIS	
mCNN [103]	T1-weighted and T2-weighted images	Brainweb NAMIC	Supervised
Novel CNN [103]	T1-weighted images	OASIS	Supervised
3D-UNet [19]	T1-weighted images	NFBS	Supervised
DSN [44]	T1-weighted images	IBSR LPBA40 and OASIS	Supervised
PSSNet [44]	T1-weighted images	Private dataset	Supervised
Complementary segmentation network for brain MRI extraction [44]	T1-weighted images	OASIS	Semi-supervised
Skull stripping using hybrid method [50]	T1-weighted and T2-weighted images	IBSR, LPBA40, and OASIS	Unsupervised

tested on normal images and pathological images. When tumors are at the boundary U-Net considered the brain tissues as non-brain. The plain U-Net over segments skull area as the brain when the intensity of skull is different. Whereas, CompNets identifies the brain region, and the optimal CompNet shows the visual results accurately. 3D-UNet [110] outperforms the conventional skull stripping methods with respect to its sensitivity, dice coefficient, and specificity. The results of 3D-UNET method have been compared with the popularly used conventional approaches BSE and ROBEX, and one is a deep-learning-based method, i.e., Kleesiek's method and 3D-UNet outperformed [110]. DSN performs well on BET for IBSR, LBPA, OASIS, and outperforms ROBEX for IBSR dataset [44].

Neuroimaging is a very sensitive and complex task. It gives researchers different types of challenges. As the brain tumor and other pathological brain disorder detection and prognosis is a very sensitive task for this purpose many pre-processing steps are followed; among them skull striping is the most important one. This paper provides classification of skull stripping techniques into conventional, machine-learning and deep-learning-based methods. Some of the challenges we highlighted through the whole process of the survey is listed below and also tried to give our opinion to the researchers. The brain scans are acquired through different imaging modalities with different contrasts, e.g., MRI and CT scans. Bain scans even acquired through MRI have multiple modalities like T1-weighted, T2-weighted, and FLAIR images. These imaging modalities have different contrasts and scan quality. Majorly skull stripping algorithms proceed only for T1-weighted MR images. Brain structures have different signal intensities, and in some cases intensities of the brain and non-brain regions like neck skull and scalp may overlap. Inhomogeneity in brain structures that vary from individual to individual is also one of the challenging task in automated skull stripping methods. To ensure the automated skull stripping methods performance in terms of some quantitative parameters like accuracy and retaining region of interest, prior noise calculation is required. Image artifacts and noise may be present, while the accusation of brain MR scans due to motion and some other noises. Selection of appropriate brain extraction method depends upon the nature of the problem and dataset, and the MRI characteristics also have a lot of influence. For accurate skull stripping many factors should be taken under consideration like scanner vendor and magnetic field intensity. Skull stripping becomes more complex in case of tumors especially when tumors are located near the border of the skull. Every method has its own merits and demerits no matter either conventional, machine, or deep-learning-based skull stripping methods. There is always a parameter for improving these methods accordingly. Keeping the above challenges in mind a quite robust automated method for stripping skull is needed that is not effected by different brain morphologies, sizes, and intensities. Since skull stripping is a preprocessing step, it must be accurate with less execution time and sufficiently robust to be helpful in both the research and clinical aspect.

Table 8 Measure of quantitative analysis of different methods of conventional skull stripping

Skull stripping methods	Groups	Methods	Quantitative analysis measures						
			Dice coefficient(DC)	Sensitivity	Specificity	Hausdorff distance(HD)	Absolute volume difference(AVD)	Mean	Jaccard coefficient (JC)
Conventional methods	Deformable surface–based models	Level sets methods	x	√	√	x	x	x	x
		Modified BET, Gaussian model, and watershed segmentation	x	√	√	x	x	x	√
		Refinement process and 3D level set	x	x	x	x	x	x	x
		Refinement process and 3D level set	x	√	√	x	x	x	√
		Improved geometric active contour	x	x	x	x	x	x	x
		Best curve selection	√	x	x	x	x	x	√
		SMHASS	√	√	√	x	x	x	√
		BET	x	x	x	x	x	√	x
		Chan-Vase; active contour model	√	x	x	x	x	x	√
	Mathematical morphological operations	3D mathematical morphology and Gauss mixture	x	x	x	x	x	x	√
		Seed growth, threshold-based method	x	x	x	x	x	x	x
		Connected component analysis and morphological operations	√	x	x	x	x	x	√
		BEA	x	x	x	x	x	x	√
		Exbrain	x	x	x	x	x	x	x
	Intensity based	Mid-sagittal brain MRI segmentation utilizing connectivity-based threshold, landmarks and anatomical information	x	x	x	x	x	x	x
		SPM2	x	x	x	x	x	x	x
		SPM5	x	x	x	x	x	x	x
		graph cuts	x	x	x	x	x	x	√
		2D region growing	√	x	x	x	x	x	√
	Template based	MAPS	x	x	x	x	x	x	√
		ANTs	x	x	x	x	x	x	x
		BEAST	√	x	x	x	x	x	x
	Hybrid methods	Adaptive segmentation, active contour, and morphological operations for brain segmentation	x	x	x	x	x	√	x
		Edge detection, adaptive anisotropic diffusion, and morphological erosions	x	x	x	x	x	x	√
		McStrip	x	x	x	x	x	x	√
		BEMA, BSE, BET, 3dintracranial, and watershed algorithm	x	x	x	x	x	√	x
		Mathematical morphology, expectation maximization (EM), connected component analysis, and 3D geodesic active contours	x	√	√	x	x	x	x
Total			6	5	5	0	0	3	13

Table 9 Measure of quantitative analysis of different methods of machine-learning-based skull stripping

Skull stripping methods	Methods	Quantitative analysis measures						
		Dice coefficient (DC)	Sensitivity	Specificity	Hausdorff distance (HD)	Absolute volume difference (AVD)	Mean	Jaccard coefficient (JC)
Machine learning methods	Fuzzy-ASM	x	√	x	x	x	x	x
	SVM classifier for skull stripping	√	x	x	x	x	x	x
	Active contour and fuzzy membership function	x	x	x	x	x	x	x
	ROBEX	√	√	√	√	x	x	x
	MASS	√	√	√	√	x	x	x
	PCA-based method	√	√	√	x	x	x	x
	Clustering and 2D region growing	√	x	x	x	x	x	√
	FLAIR axial method of skull stripping	√	x	x	x	x	x	x
Total		6	4	3	2	0	0	1

A fully automated method covers all the above-mentioned challenges and will be able to develop a method that strips the skull automatically and be able to perform well on the multiple morphologies of the brain. When dealing with less data conventional techniques can work well for more robust and appropriate results machine learning and deep learning approaches are used as the medical data are too big, so deep learning approaches perform so well. Deep learning approaches have been raised as a front-runner in the field of neuroimaging, so, the researchers new to this field should spend more time in the deep learning domain. As the results of skull stripping methods using deep learning outperform many other techniques of conventional and machine learning approaches. In medical image analysis algorithms, the deep learning paradigm shows outstanding performance. The accuracy of deep learning network is higher than classical approaches of machine learning. Additionally, greater the data more will be the performance of deep networks as compared to conventional machine learning with complex algorithms as mentioned in [19]. The trainings of deep learning approaches are much data-hungry and time-consuming.The training of deep learning approaches is time-consuming and data-hungry. Therefore, such learning algorithms require parallel processing tools, like Graphics Processing Units (GPUs), to

Table 10 Measure of quantitative analysis of different methods of deep-learning-based skull stripping

Skull stripping methods	Methods	Quantitative analysis measures						
		Dice coefficient (DC)	Sensitivity	Specificity	Hausdorff distance (HD)	Absolute volume difference (AVD)	Mean	Jaccard coefficient (JC)
Deep learning methods	Auto-Net	√	√	√	x	X	x	x
	3D CNN	√	√	√	x	x	x	x
	MONSTR	√	x	x	x	x	x	x
	VoxResNet	√	x	x	√	√	x	x
	CNN Consensus-based Silver Standards Masks	√	√	√	√	x	√	x
	ASM-CNN	√	√	√	√	x	x	√
	Multistable cellular CNN	√	x	x	x	x	x	√
	DSN	√	√	√	√	x	x	x
	PSSNet	√	√	√	x	x	x	x
	CompNets	√	√	√	x	x	x	x
Total		11	8	8	4	1	1	2

accelerate the training process of such a larger dataset [111]. To lessen the computational cost of deep learning methods few architectures are used like Mobilenet, Xception, and GoogleNet that decrease the computational time of deep learning methods. As it is quite evident through the survey that majority of the skull stripping methods are generally applicable on T1-weighted brain MR images, such a robust model is required in future that is capable of working and showing near to perfect results for all the MR modalities like T1-weighted, T2-weighted, and FLAIR images. In neuroimaging processing and identification skull stripping is considered as a demanding research field providing researchers with a vast area to study and help radiologists and neurologists. In order to skull strip well in case of brain scans with a tumor near the skull boundary, more detection of features is required that carefully check the shape deformities and intensities so closely and accurately.

Model of Quantitative Analysis Measures Based on Skull Stripping Methods

This section contains a model of different quantifying parameters being used in the study of skull stripping. Various quantifying parameters are used for the accurate analysis of skull stripping, and the most frequently used are dice coefficient (DC), sensitivity, and specificity. The following Table 8 describes the analysis of quantitative measures of conventional skull stripping methods in detail.

Table 9 gives the detailed analysis of quantitative parameters used in case of machine-learning-based skull stripping methods.

The analysis of quantitative measures for deep-learning-based skull stripping methods is depicted in the following Table 10.

The above Tables 8, 9, and 10 give the detailed analysis of quantitative measures of conventional, machine, and deep-learning-based skull stripping methods. According to the above analysis the most accurate quantitative measures are DC, sensitivity, specificity, and JC. The total number of research articles in this survey that used them are 23, 17, 16, and 14, respectively. The other less frequently used quantitative measures found in research articles are HD, AVD, and mean; the number of research articles considering them are 6, 1, and 4, respectively. Based on the assessment of related literature, it is observed that the quantitative analysis is influenced by the system technology, skull stripping method, and context. Thus, an insight is presented to propose quantifying parameters used in skull stripping. Figure 8 shows the model of quantifying parameters frequently used in skull stripping methods.

Additionally, designers and developers need to fully understand these contextual factors and determine which quantifying parameters are considered appropriate for the design

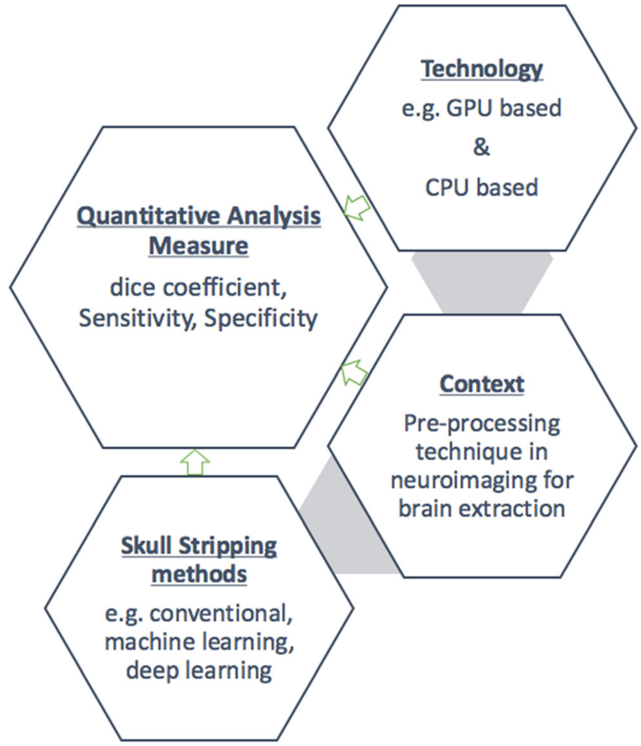


Fig. 8 Model of quantifying parameters used in skull stripping

process and the evaluation of the system. For this reason, it is important to determine the core quantifying parameters in term of skull stripping. Initially, these parameters are cross-verified by well-known skull stripping methods in the field of conventional , machine learning, and deep learning methods. Likewise, reviews are performed to determine parameters that evaluate existing skull stripping techniques. The findings present three parameters that are necessary for the evaluation of skull stripping. It means that the parameters are measured, which are strongly influenced by contextual factors. The quantifying parameters include data coefficient, sensitivity, and specificity. Dice coefficient (DC) describes the similarity level between the algorithm of skull stripping or segmentation results and ground truth. Sensitivity is the actual proportion of correctly identified positives. Specificity is the measure of correctly identified proportion of actual negatives.

Conclusion and Future Work

An elaborated survey of the existing conventional and state-of-the-art automated machine and deep-learning-based skull stripping techniques are discussed in this paper. Here the aim is to introduce current skull stripping algorithms at one platform. It is a significant pre-processing step in analyzing brain MRI and differentiating between the brain and skull portion. In many neuroimaging processes, the importance of the skull stripping step cannot be denied, and once achieved, it increases the computational speed of the neuro-based algorithms, as the brain images are acquired using different imaging modalities. Hence, every time the brain images are with varying contrast, scan quality, and intensities inhomogeneity, this makes the skull stripping a challenging task. Different stripping algorithms are proposed, i.e., manual, semi-automated, and automated algorithms. Automated skull stripping increases the accuracy and efficiency of many neuroimaging algorithms. The current deep-learning-based skull stripping algorithm results are more precise and accurate than the conventionally existing techniques.

In future, there is a need to develop state-of-the-art robust and optimized fully automated supervised or unsupervised skull stripping algorithm that fulfills all the lope holes of the previously existing techniques. The novel skull stripping method should provide all the possible solutions for the challenges of skull stripping methods. Brain MRIs can be used for the identification of pathological disorders in future, so, there is a need to optimize the network that decreases the computational complexity. As the majority of skull stripping algorithms proceeds only for T1 weighted MR images, to increase the output accuracy it is expected to use the multiple modalities, like FLAIR, T1 and T2 weighted brian MR images along with their training data sets. Moreover, the novel method should also be able to work on multiple brain orientations and acquisition sequences without parameters adjusting.

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References

1. D. Purves et al., Eds., Neuroscience, 4th ed. Sunderland, MA, US: Sinauer Associates, 2008.
2. H. Blumenfeld, Neuroanatomy through Clinical Cases, 2nd ed. 2010.
3. R. M. Quencer and W. G. Bradley, MR imaging of the brain: what constitutes the minimum acceptable capability?, AJNR. Am. J. Neuroradiol., vol. 22, no. 8, pp. 1449–50, 2001.
4. M. Cheour, Advantages of brain MRI, Radiol. Org, 2010.
5. M. Ben Salah, I. Diaz, R. Greiner, P. Boulanger, B. Hoehn, and A. Murtha, Fully automated brain tumor segmentation using two mri modalities, in International Symposium on Visual Computing, 2013, pp. 30–39.
6. Z. Akkus, A. Galimzianova, A. Hoogi, D. L. Rubin, and B. J. Erickson, Deep learning for brain MRI segmentation: state of the art and future directions, J. Digit. Imaging, vol. 30, no. 4, pp. 449–459, 2017.
7. K. Kazemi and N. Noorizadeh, Quantitative comparison of SPM, FSL, and brainsuite for brain MR image segmentation, J. Biomed. Phys. Eng., vol. 4, no. 1, p. 13, 2014.
8. A. Chaddad and C. Tanougast, Quantitative evaluation of robust skull stripping and tumor detection applied to axial MR images, Brain informatics, vol. 3, no. 1, pp. 53–61, 2016.
9. R. Nilakant, H. P. Menon, and K. Vikram, A survey on advanced segmentation techniques for brain MRI image segmentation, Int. J. Adv. Sci. Eng. Inf. Technol., vol. 7, no. 4, pp. 1448–1456, 2017.
10. H. Huang, F. Meng, S. Zhou, F. Jiang, and G. Manogaran, Brain image segmentation based on FCM clustering algorithm and rough set, IEEE Access, vol. 7, pp. 12386–12396, 2019.
11. I. Despotović, B. Goossens, and W. Philips, MRI segmentation of the human brain: challenges, methods, and applications, Comput. Math. Methods Med., vol. 2015, 2015.
12. A. Khan, A. Sohail, U. Zahoora, and A. S. Qureshi, A survey of the recent architectures of deep convolutional neural networks, arXiv Prepr. arXiv1901.06032, 2019.
13. F. Hosseini, H. Ebrahimpourkomleh, and M. KhodamHazrati, Quantitative evaluation of skull stripping techniques on magnetic resonance images, in World Congress on Electrical Engineering and Computer Systems and Science (EECSS 2015).
14. Y. Wang, J. Nie, P.-T. Yap, F. Shi, L. Guo, and D. Shen, Robust deformable-surface-based skull-stripping for large-scale studies, in International Conference on Medical Image Computing and Computer-Assisted Intervention, 2011, pp. 635–642.
15. A. M. Dale, B. Fischl, and M. I. Sereno, Cortical surface-based analysis: I. Segmentation and surface reconstruction, Neuroimage, vol. 9, no. 2, pp. 179–194, 1999.
16. D. W. Shattuck, S. R. Sandor-Leahy, K. A. Schaper, D. A. Rottenberg, and R. M. Leahy, Magnetic resonance image tissue classification using a partial volume model, Neuroimage, vol. 13, no. 5, pp. 856–876, 2001.
17. S. F. Eskildsen et al., BEaST: Brain extraction based on nonlocal segmentation technique, Neuroimage, vol. 59, no. 3, pp. 2362–2373, 2012.
18. H. K. Hahn and H.-O. Peitgen, The skull stripping problem in MRI solved by a single 3D watershed transform BT—Medical Image Computing and Computer-Assisted Intervention—MICCAI 2000, 2000, pp. 134–143.
19. H. Hwang, Z. H. Rehman, and S. Lee, 3D U-Net for skull stripping in brain MRI, Appl. Sci., vol. 9, no. 3, 2019.
20. J. E. Iglesias, C. Liu, P. M. Thompson, and Z. Tu, Robust brain extraction across datasets and comparison with publicly available methods, IEEE Trans. Med. Imaging, vol. 30, no. 9, pp. 1617–1634, 2011.
21. P. A. V Miranda, F. A. M. Cappabianco, and J. S. Ide, A case analysis of the impact of prior center of gravity estimation over skull-stripping algorithms in MR images, in 2013 IEEE International Conference on Image Processing, 2013, pp. 675–679.
22. C. Baillard, P. Hellier, and C. Barillot, Segmentation of brain 3D MR images using level sets and dense registration, Med. Image Anal., vol. 5, no. 3, pp. 185–194, 2001.
23. S. M. Smith, Fast robust automated brain extraction, Hum. Brain Mapp., vol. 17, no. 3, pp. 143–155, 2002.
24. J. Qiu and C. Wenqiang, Brain tissues extraction based on improved Brain Extraction Tool algorithm, in 2016 2nd IEEE International Conference on Computer and Communications, ICCC 2016 - Proceedings, 2017, pp. 553–556.
25. V. Popescu et al., Optimizing parameter choice for FSL-Brain Extraction Tool (BET) on 3D T1 images in multiple sclerosis, Neuroimage, vol. 61, no. 4, pp. 1484–1494, 2012.
26. J. Muschelli, N. L. Ullman, W. A. Mould, P. Vespa, D. F. Hanley, and C. M. Crainiceanu, Validated automatic brain extraction of head CT images, Neuroimage, vol. 114, pp. 379–385, 2015.
27. M. Jenkinson, M. Pechaud, and S. Smith, BET2: MR-based estimation of brain, skull and scalp surfaces, in Eleventh annual

meeting of the organization for human brain mapping, 2005, vol. 17, p. 167.
28. M. Jenkinson, P. Bannister, M. Brady, and S. Smith, Improved optimization for the robust and accurate linear registration and motion correction of brain images, Neuroimage, vol. 17, no. 2, pp. 825–841, 2002.
29. AFNI program: 3dSkullStrip. [Online]. Available: https://afni.nimh.nih.gov/pub/dist/doc/program_help/3dSkullStrip.html. [Accessed: 10-Nov-2019].
30. C. Yunjie, Z. Jianwei, and W. Shunfeng, A new fast brain skull stripping method, biomedical engineering and informatics, in Proc. 2nd International Conference on Biomedical Engineering and Informatics, BMEI09, Tianjin, 2009.
31. J.-X. Liu, Y.-S. Chen, and L.-F. Chen, Accurate and robust extraction of brain regions using a deformable model based on radial basis functions, J. Neurosci. Methods, vol. 183, no. 2, pp. 255–266, 2009.
32. H. Merisaari et al., Gaussian mixture model-based segmentation of MR images taken from premature infant brains, J. Neurosci. Methods, vol. 182, no. 1, pp. 110–122, 2009.
33. K. Somasundaram and P. Kalavathi, Skull stripping of MRI head scans based on Chan-Vese active contour model, Int. J. Knowl. Manag. e-learning, vol. 3, no. 1, pp. 7–14, 2011.
34. X. Tao and M.-C. Chang, A skull stripping method using deformable surface and tissue classification, in Medical Imaging 2010: Image Processing, 2010, vol. 7623, p. 76233L.
35. H. Zhang, J. Liu, Z. Zhu, and H. Li, An automated and simple method for brain MR image extraction, Biomed. Eng. Online, vol. 10, no. 1, p. 81, 2011.
36. K. Somasundaram and R. Siva Shankar, A novel skull stripping method for T1 coronal and T2 axial magnetic resonance images of human head scans based on resonance principle, in Proceedings of the 2012 International Conference on Image Processing, Computer Vision, and Pattern Recognition, IPCV 2012, 2012, vol. 1, pp. 29–35.
37. F. J. Galdames, F. Jaillet, and C. A. Perez, An accurate skull stripping method based on simplex meshes and histogram analysis for magnetic resonance images, J. Neurosci. Methods, vol. 206, no. 2, pp. 103–119, 2012.
38. X. Zeng, L. H. Staib, R. T. Schultz, and J. S. Duncan, Segmentation and measurement of the cortex from 3-D MR images using coupled-surfaces propagation, IEEE Trans. Med. Imaging, vol. 18, no. 10, pp. 927–937, 1999.
39. J. Hwang, Y. Han, and H. Park, Skull-stripping method for brain MRI using a 3D level set with a speedup operator, J. Magn. Reson. Imaging, vol. 34, no. 2, pp. 445–456, 2011.
40. Z. Lao, D. Shen, and C. Davatzikos, Statistical shape model for automatic skull-stripping of brain images, in Proceedings IEEE International Symposium on Biomedical Imaging, 2002, pp. 855–858.
41. B. D. Ward, 3dIntracranial: Automatic segmentation of intracranial region, Tech. Report, Biophys. Res. Institute, Med. Coll. Wisconsin, UK, 1999.
42. G. B. Aboutanos, J. Nikanne, N. Watkins, and B. M. Dawan, Model creation and deformation for the automatic segmentation of the brain in MR images, IEEE Trans. Biomed. Eng., vol. 46, no. 11, pp. 1346–1356, 1999.
43. Y. Gao et al., A multi-view pyramid network for skull stripping on neonatal T1-weighted MRI, Magn. Reson. Imaging, vol. 63, pp. 70–79, 2019.
44. A. Sikka, G. Mittal, D. R. Bathula, and N. C. Krishnan, Supervised deep segmentation network for brain extraction, in Proceedings of the Tenth Indian Conference on Computer Vision, Graphics and Image Processing, 2016, p. 9.
45. C. Tsai, B. S. Manjunath, and bio3R Jagadeesan, Automated segmentation of brain MR images, Pattern Recognit., vol. 28, no. 12, pp. 1825–1837, 1995.
46. K. J. Shanthi and M. S. Kumar, Skull stripping and automatic segmentation of brain MRI using seed growth and threshold techniques, in 2007 International Conference on Intelligent and Advanced Systems, 2007, pp. 422–426.
47. S. Mohsin, S. Sajjad, Z. Malik, and A. H. Abdullah, Efficient way of skull stripping in MRI to detect brain tumor by applying morphological operations, after detection of false background, Int. J. Inf. Educ. Technol., vol. 2, no. 4, p. 335, 2012.
48. L. Lemieux, G. Hagemann, K. Krakow, and F. G. Woermann, Fast automatic segmentation of the brain in T1-weighted volume MRI data, in Medical Imaging 1999: Image Processing, 1999, vol. 3661, pp. 152–160.
49. A. Mikheev, G. Nevsky, S. Govindan, R. Grossman, and H. Rusinek, Fully automatic segmentation of the brain from T1-weighted MRI using Bridge Burner algorithm, J. Magn. Reson. Imaging, vol. 27, no. 6, pp. 1235–1241, 2008.
50. K. Somasundaram and P. Kalavathi, A hybrid method for automatic skull stripping of magnetic resonance images (MRI) of human head scans, 2010 2nd Int. Conf. Comput. Commun. Netw. Technol. ICCCNT 2010, pp. 1–5, 2010.
51. J. R. Hesselink, Basic principles of MR imaging, Department of Radiology, University of California. 2009.
52. K. Somasundaram and T. Kalaiselvi, Fully automatic brain extraction algorithm for axial T2-weighted magnetic resonance images, Comput. Biol. Med., vol. 40, no. 10, pp. 811–822, 2010.
53. M. E. Brummer, R. M. Mersereau, R. L. Eisner, and R. R. J. Lewine, Automatic detection of brain contours in MRI data sets, IEEE Trans. Med. Imaging, vol. 12, no. 2, pp. 153–166, 1993.
54. J. Gao and M. Xie, Skull-stripping MR brain images using anisotropic diffusion filtering and morphological processing, in 2009 International Symposium on Computer Network and Multimedia Technology, 2009, pp. 1–4.
55. R. W. Cox, AFNI: software for analysis and visualization of functional magnetic resonance neuroimages, Comput. Biomed. Res., vol. 29, no. 3, pp. 162–173, 1996.
56. S. Huh, T. A. Ketter, K. H. Sohn, and C. Lee, Automated cerebrum segmentation from three-dimensional sagittal brain MR images, Comput. Biol. Med., vol. 32, no. 5, pp. 311–328, 2002.
57. H. Suzuki and Jichiro Toriwaki, Automatic segmentation of head mri images by knowledge guided thresholding, Comput. Med. Imaging Graph., vol. 15, no. 4, pp. 233–240, 1991.
58. B. M. Dawant, S. L. Hartmann, J.-. Thirion, F. Maes, D. Vandermeulen, and P. Demaerel, Automatic 3-D segmentation of internal structures of the head in MR images using a combination of similarity and free-form transformations. I. Methodology and validation on normal subjects, IEEE Trans. Med. Imaging, vol. 18, no. 10, pp. 909–916, 1999.
59. D. L. Pham and J. L. Prince, Adaptive fuzzy segmentation of magnetic resonance images, IEEE Trans. Med. Imaging, vol. 18, no. 9, pp. 737–752, 1999.
60. G. B. Aboutanos and B. M. Dawant, Automatic brain segmentation and validation: image-based versus atlas-based deformable models, in Proc.SPIE, 1997, vol. 3034.
61. M. S. Atkins and B. T. Mackiewich, Fully automatic segmentation of the brain in MRI, IEEE Trans. Med. Imaging, vol. 17, no. 1, pp. 98–107, 1998.
62. K. Somasundaram and T. Kalaiselvi, Automatic brain extraction methods for T1 magnetic resonance images using region labeling and morphological operations, Comput. Biol. Med., vol. 41, no. 8, pp. 716–725, 2011.
63. S. S. R and K. Somasundaram, Automatic skull stripping using maxima-minima value from quadratic equations for MR images, vol. 5, no. Xii, pp. 647–657, 2017.

64. G. Fein et al., Statistical parametric mapping of brain morphology: sensitivity is dramatically increased by using brain-extracted images as inputs, Neuroimage, vol. 30, no. 4, pp. 1187–1195, 2006.
65. A. Klein et al., Evaluation of 14 nonlinear deformation algorithms applied to human brain MRI registration, Neuroimage, vol. 46, no. 3, pp. 786–802, 2009.
66. Z. Y. Shan, G. H. Yue, and J. Z. Liu, Automated histogram-based brain segmentation in T1-weighted three-dimensional magnetic resonance head images, Neuroimage, vol. 17, no. 3, pp. 1587–1598, 2002.
67. V. Grau, A. U. J. Mewes, M. Alcaniz, R. Kikinis, and S. K. Warfield, Improved watershed transform for medical image segmentation using prior information, IEEE Trans. Med. Imaging, vol. 23, no. 4, pp. 447–458, 2004.
68. P. Kalavathi and V. B. S. Prasath, Methods on skull stripping of MRI head scan images—a review, Journal of Digital Imaging, vol. 29, no. 3. Springer New York LLC, pp. 365–379, 01-Jun-2016.
69. S. A. Sadananthan, W. Zheng, M. W. L. Chee, and V. Zagorodnov, Skull stripping using graph cuts, Neuroimage, vol. 49, no. 1, pp. 225–239, 2010.
70. P. Kalavathi and V. B. S. Prasath, Methods on skull stripping of MRI head scan images—a review, J. Digit. Imaging, vol. 29, no. 3, pp. 365–379, 2016.
71. K. Somasundaram and P. Kalavathi, Skull stripping from MRI of head scans based on 2D region growing.
72. K. Somasundaram and P. Kalavathi, “Skull stripping of MRI head scans based on chan-vese active contour model,” Int J Knowl Manag elearning, vol. 3, no. 1, pp. 7–14, 2011.
73. K. Somasundaram and P. Kalavathi, Brain segmentation in magnetic resonance human head scans using multi-seeded region growing, Imaging Sci. J., vol. 62, no. 5, pp. 273–284, 2014
74. S. Roy, J. A. Butman, and D. L. Pham, Robust skull stripping using multiple MR image contrasts insensitive to pathology, Neuroimage, vol. 146, pp. 132–147, 2017.
75. K. K. Leung et al., Brain MAPS: An automated, accurate and robust brain extraction technique using a template library, Neuroimage, vol. 55, no. 3, pp. 1091–1108, 2011.
76. B. B. Avants, N. J. Tustison, M. Stauffer, G. Song, B. Wu, and J. C. Gee, The insight ToolKit image registration framework, Frontiers in Neuroinformatics, vol. 8. p. 44, 2014.
77. R. A. Heckemann et al., Brain extraction using label propagation and group agreement:Pincram, PLoS One, vol. 10, no. 7, p. e0129211, 2015.
78. F. Ségonne et al., A hybrid approach to the skull stripping problem in MRI, Neuroimage, vol. 22, no. 3, pp. 1060–1075, 2004.
79. T. Kapur, W. E. L. Grimson, W. M. Wells, and R. Kikinis, Segmentation of brain tissue from magnetic resonance images, Med. Image Anal., vol. 1, no. 2, pp. 109–127, 1996.
80. W. M. Wells, W. Grimson, R. Kikinis, and F. A. Jolesz, Adaptive segmentation of MRI data, in Lecture notes in computer science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics), 1995, vol. 905, pp. 59–69.
81. D. E. Rex et al., A meta-algorithm for brain extraction in MRI, Neuroimage, vol. 23, no. 2, pp. 625–637, 2004.
82. A. Huang, R. Abugharbieh, R. Tam, and A. Traboulsee, MRI brain extraction with combined expectation maximization and geodesic active contours, in 2006 IEEE International Symposium on Signal Processing and Information Technology, 2006, pp. 107–111.
83. S. Bauer, T. Fejes, and M. Reyes, A skull-stripping filter for ITK, Insight J., pp. 1–7, 2012.
84. M. D. Abràmoff, P. J. Magalhães, and S. J. Ram, Image Processing with ImageJ, vol. 11, no. 7. 2004.
85. K. Rehm, K. Schaper, J. Anderson, R. Woods, S. Stoltzner, and D. Rottenberg, Putting our heads together: a consensus approach to brain/non-brain segmentation in T1-weighted MR volumes, Neuroimage, vol. 22, no. 3, pp. 1262–1270, 2004.
86. A. H. Zhuang, D. J. Valentino, and A. W. Toga, Skull-stripping magnetic resonance brain images using a model-based level set, Neuroimage, vol. 32, no. 1, pp. 79–92, 2006.
87. J. S. Suri, Two-dimensional fast magnetic resonance brain segmentation, IEEE Eng. Med. Biol. Mag., vol. 20, no. 4, pp. 84–95, 2001.
88. S. Kobashi et al., Fuzzy-ASM based automated skull stripping method from infantile brain MR images, in 2007 IEEE International Conference on Granular Computing (GRC 2007), 2007, p. 632.
89. J. Sjölund, A. E. Järlideni, M. Andersson, H. Knutsson, and H. Nordström, Skull segmentation in MRI by a support vector machine combining local and global features, in 2014 22nd International Conference on Pattern Recognition, 2014, pp. 3274–3279.
90. X. Han et al., Brain extraction from normal and pathological images: a joint PCA/Image-Reconstruction approach, Neuroimage, vol. 176, pp. 431–445, 2018.
91. J. Doshi, G. Erus, Y. Ou, B. Gaonkar, and C. Davatzikos, Multi-atlas skull-stripping, Acad. Radiol., vol. 20, no. 12, pp. 1566–1576, 2013.
92. A. Maier, C. Syben, T. Lasser, and C. Riess, A gentle introduction to deep learning in medical image processing, Z. Med. Phys., vol. 29, no. 2, pp. 86–101, 2019.
93. S. W. Hartley, A. I. Scher, E. S. C. Korf, L. R. White, and L. J. Launer, Analysis and validation of automated skull stripping tools: a validation study based on 296 MR images from the Honolulu Asia aging study, Neuroimage, vol. 30, no. 4, pp. 1179–1186, 2006.
94. J. Kleesiek et al., Deep MRI brain extraction: a 3D convolutional neural network for skull stripping, Neuroimage, vol. 129, pp. 460–469, 2016.
95. S. S. M. Salehi, D. Erdogmus, and A. Gholipour, Auto-Context Convolutional Neural Network (Auto-Net) for brain extraction in magnetic resonance imaging, IEEE Trans. Med. Imaging, vol. 36, no. 11, pp. 2319–2330, 2017.
96. E. Shelhamer, J. Long, and T. Darrell, Fully convolutional networks for semantic segmentation, IEEE Trans. Pattern Anal. Mach. Intell., vol. 39, no. 4, pp. 640–651, 2017.
97. H. Chen, Q. Dou, L. Yu, J. Qin, and P.-A. Heng, VoxResNet: deep voxelwise residual networks for brain segmentation from 3D MR images, Neuroimage, vol. 170, pp. 446–455, 2018.
98. K. Kamnitsas et al., Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation, Med. Image Anal., vol. 36, pp. 61–78, 2017.
99. O. Lucena, R. Souza, L. Rittner, R. Frayne, and R. Lotufo, Silver standard masks for data augmentation applied to deep-learning-based skull-stripping, in 2018 IEEE 15th International Symposium on Biomedical Imaging (ISBI 2018), 2018, pp. 1114–1117.
100. O. Lucena, R. Souza, L. Rittner, R. Frayne, and R. Lotufo, Convolutional neural networks for skull-stripping in brain MR imaging using Consensus-based Silver standard Masks, arXiv Prepr. arXiv1804.04988, 2018.
101. Z. Tu and X. Bai, Auto-context and its application to high-level vision tasks and 3D brain image segmentation, IEEE Trans. Pattern Anal. Mach. Intell., vol. 32, no. 10, pp. 1744–1757, 2010.
102. N. H. M. Duy, N. M. Duy, M. T. N. Truong, P. T. Bao, and N. T. Binh, Accurate brain extraction using active shape model and convolutional neural networks, arXiv Prepr. arXiv1802.01268, 2018.
103. B. Yilmaz, A. Durdu, and G. D. Emlik, A new method for skull stripping in brain MRI using multistable cellular neural networks, Neural Comput. Appl., vol. 29, no. 8, pp. 79–95, 2018.

104. R. Dey and Y. Hong, CompNet: Complementary Segmentation Network for brain MRI extraction, in International Conference on Medical Image Computing and Computer-Assisted Intervention, 2018, pp. 628–636.
105. S. Tchoketch Kebir, S. Mekaoui, and M. Bouhedda, A fully automatic methodology for MRI brain tumour detection and segmentation, Imaging Sci. J., vol. 67, no. 1, pp. 42–62, 2019.
106. N. H. M. Duy, N. M. Duy, M. T. N. Truong, P. T. Bao, and N. T. Binh, “Accurate brain extraction using Active Shape Model and Convolutional Neural Networks,” Feb. 2018.
107. K. Boesen et al., Quantitative comparison of four brain extraction algorithms, Neuroimage, vol. 22, no. 3, pp. 1255–1261, 2004.
108. C. Fennema-Notestine et al., Quantitative evaluation of automated skull-stripping methods applied to contemporary and legacy images: effects of diagnosis, bias correction, and slice location, Hum. Brain Mapp., vol. 27, no. 2, pp. 99–113, 2006.
109. S. K. Warfield, K. H. Zou, and W. M. Wells, Simultaneous truth and performance level estimation (STAPLE): an algorithm for the validation of image segmentation, IEEE Trans. Med. Imaging, vol. 23, no. 7, pp. 903–921, 2004.
110. S. Tchoketch Kebir, S. Mekaoui, and M. Bouhedda, “A fully automatic methodology for MRI brain tumour detection and segmentation,” Imaging Sci. J., vol. 67, no. 1, pp. 42–62, 2019.
111. M. K. Abd-Ellah, A. I. Awad, A. A. M. Khalaf, and H. F. A. Hamed, Two-phase multi-model automatic brain tumour diagnosis system from magnetic resonance images using convolutional neural networks, EURASIP J. Image Video Process., vol. 2018, no. 1, p. 97, 2018.
112. Kashyap, V., Li, J. Skull stripping axial FLAIR MRIs of the brain using machine learning
113. Kavitha Srinivasan, N. N. (2018). An intelligent skull stripping algorithm for MRI image sequences using mathematical morphology
114. R. Souza et al., An open, multi-vendor, multi-field-strength brain MR dataset and analysis of publicly available skull stripping methods agreement, NeuroImage, vol. 170. Academic Press Inc., pp. 482–494, 15-Apr-2018.
115. O. Lucena, R. Souza, L. Rittner, R. Frayne, and R. Lotufo, Convolutional neural networks for skull-stripping in brain MR imaging using silver standard masks, Artif. Intell. Med., vol. 98, pp. 48–58, 2019.
116. S. Roy, D. Bhattacharyya, S. K. Bandyopadhyay, and T.-H. Kim, Artifacts and skull stripping: an application towards the preprocessing for brain abnormalities detection from MRI, Int. J. Control Autom., vol. 10, no. 5, pp. 147–160, 2017.
117. Q. Zhang, L. Wang, X. Zong, W. Lin, G. Li, and D. Shen, Frnet: Flattened residual network for infant MRI skull stripping, in Proceedings - International Symposium on Biomedical Imaging, 2019, vol. 2019-April, pp. 999–1002.
118. A. Fedorov, J. Johnson, E. Damaraju, A. Ozerin, V. Calhoun, and S. Plis, End-to-end learning of brain tissue segmentation from imperfect labeling, Proc. Int. Jt. Conf. Neural Networks, vol. 2017-May, pp. 3785–3792, 2017.
119. Y. Huo et al., 3D whole brain segmentation using spatially localized atlas network tiles, Neuroimage, vol. 194, pp. 105–119, 2019.
120. K. Chen, J. Shen, and F. Scalzo, Skull stripping using confidence segmentation convolution neural network, in Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics), 2018, vol. 11241 LNCS, pp. 15–24.
121. A. B. Waters, R. A. Mace, K. S. Sawyer, and D. A. Gansler, Identifying errors in Freesurfer automated skull stripping and the incremental utility of manual intervention, Brain Imaging Behav., vol. 13, no. 5, pp. 1281–1291, 2019.
122. Z. Liu, B. Xiao, Y. Li, and Y. Fan, Context-endcoding for neural network-based skull stripping in magnetic resonance imaging, 2019.
123. C. G. B. Yogananda, B. C. Wagner, G. K. Murugesan, A. Madhuranthakam, and J. A. Maldjian, A deep learning pipeline for automatic skull stripping and brain segmentation, in Proceedings - International Symposium on Biomedical Imaging, 2019, vol. 2019-April, pp. 727–731.
124. S. Thakur et al., NIMG-40. Robust modality-agnostic skull-stripping in presence of diffuse glioma: a multi-institutional study, Neuro. Oncol., vol. 21, no. Supplement_6, pp. vi170–vi170, 2019.
125. N. E. Leal Narváez and E. E. Zurek Varela, A new approach on skull stripping of brain MRI based on saliency detection using dictionary learning and sparse coding, Prospectiva, vol. 17, no. 2, 2019.
126. H. Z. U. Rehman, Fully automatic and efficient midsagittal plane extraction, alignment, and skull stripping in neuroimages, 한 대학교, 2019.
127. M. Uhlich et al., Improved brain tumor segmentation via registration-based brain extraction, Forecasting, vol. 1, no. 1, pp. 59–69, 2018.
128. P. E. Yoo et al., Optimized partial-coverage functional analysis pipeline (OPFAP): a semi-automated pipeline for skull stripping and co-registration of partial-coverage, ultra-high-field functional images, Magn. Reson. Mater. Physics, Biol. Med., vol. 31, no. 5, pp. 621–632, 2018.