



Published in final edited form as:

*Acad Radiol.* 2019 December ; 26(12): 1695–1706. doi:10.1016/j.acra.2019.07.006.

## Automated Segmentation of Tissues using CT and MRI: A Systematic Review

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### Abstract

The automated segmentation of organs and tissues throughout the body using computed tomography (CT) and magnetic resonance imaging (MRI) has been rapidly increasing. Research

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into many medical conditions has benefited greatly from these approaches by allowing the development of more rapid and reproducible quantitative imaging markers. These markers have been used to help diagnose disease, determine prognosis, select patients for therapy, and follow responses to therapy. Because some of these tools are now transitioning from research environments to clinical practice, it is important for radiologists to become familiar with various methods used for automated segmentation. The Radiology Research Alliance of the Association of University Radiologists convened an Automated Segmentation Task Force to conduct a systematic review of the peer-reviewed literature on this topic. The systematic review presented here includes 408 studies and discusses various approaches to automated segmentation using CT and MRI for neurologic, thoracic, abdominal, musculoskeletal, and breast imaging applications. These insights should help prepare radiologists to better evaluate automated segmentation tools and apply them not only to research, but eventually to clinical practice.

### Keywords

segmentation; machine learning; quantitative imaging; CT; MRI

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### Introduction

Various approaches to automated segmentation of CT and MR images are widely used in research environments and promise to transform clinical practice [1–12]. Radiologists involved in interpreting images in patients with cancer, obesity, cardiovascular disease, neurodegeneration, osteoporosis, arthritis, and many other conditions will benefit from these approaches as they help clinicians diagnose disease, determine prognosis, select patients for therapy, and follow responses to therapy. To enable this transition from research to patient care, radiologists should become familiar with various methods used for automated segmentation of CT and MR images.

Segmentation refers to identifying the boundaries of an object in the image. Frequently, the object is an organ, a tissue, a pathologic lesion, or another structure used for diagnosis or management of a particular disease. Traditional approaches to segmentation rely on manual or semi-automated delineation of the object of interest. While these approaches are effective, they are time-consuming and impractical for large scale research studies and even less practical for clinical practice. As a result, many fully automated approaches to tissue segmentation are being developed.

Automated segmentation methods using CT and MRI are generally built on basic image processing of pixel intensities and/or textural features (e.g., relationships between groups of pixels), and may incorporate advanced model-based, atlas-based, or machine learning (ML) techniques [13–16]. Segmentation techniques can be broadly divided into supervised and unsupervised.

Supervised techniques require prior training that is most commonly performed manually. These methods typically include pre-processing such as intensity normalization (e.g., histogram-based, reference tissue), followed by classification (e.g., artificial neural networks,  $k$ -nearest neighbors, Bayesian, random decision forests), and feature selection

based on intensity, spatial, texture, or contextual information [13–16]. They are considered to be more accurate, but require expert annotation which is both expensive and time consuming.

Unsupervised segmentation techniques do not require any training and are generally considered less accurate than supervised techniques. These methods usually incorporate clustering (e.g., fuzzy c-means, expectation-maximization) and spatial information (e.g., Markov random fields, graph cut, anatomical/topological atlases) to segment the image [13–16]. They also commonly rely on labeled atlases.

The reported performance of supervised and unsupervised segmentation techniques varies greatly, depending in part on the validation metrics used [13–16]. Generally, the validation is based on the assessment by experts. Since evaluation by a single expert may be biased, some studies employ multiple experts using techniques such as Simultaneous Truth and Performance Level Estimation (STAPLE) [17]. In some cases, the segmentation techniques are validated against established pipelines, such as FreeSurfer (<https://surfer.nmr.mgh.harvard.edu/>), SPM (<https://www.fil.ion.ucl.ac.uk/spm/>), or FSL (<https://www.fmrib.ox.ac.uk/fsl>). Another approach uses publically available “challenge databases” for training and validation of automated segmentation techniques.

Many validation metrics have been used for quantitative comparison between the automated segmentation results and ground truth [12–16]. These metrics include: Dice similarity coefficient (DSC), Jaccard index, volume difference, Hausdorff distance, intraclass correlation, and Pearson’s coefficient. The DSC calculates the overlap between two binary segmentation results by accounting for both the intersection and the union of the two results. More familiar metrics are also occasionally used, including: sensitivity, specificity, accuracy, positive predictive value, and negative predictive value.

Previous reviews of segmentation have focused on CT or MRI of a single body region, often combining semi-automated and automated approaches, and rarely using the methodologic rigor of a systematic review. There is a need for a systematic review that focuses on automated segmentation using CT and MRI of the entire body.

We provide such a systematic review of the automated segmentation methods and discuss how these methods have been used in neurologic, thoracic, abdominal, musculoskeletal, and breast imaging. Ultimately, we hope to prepare radiologists for eventual integration of these techniques into their clinical practice.

## Methods

### Identification of Studies

This systematic review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines [18]. A systematic literature search was conducted in the PubMed/MEDLINE, Embase via Ovid, and Cochrane Central Register of Controlled Trials (CENTRAL) via Ovid databases from January 1, 2007 through February 26, 2018 (date of final search execution). A list of Medical Subject

Headings (MeSH) and keywords targeting full-text, automated segmentation using CT or MRI was formulated by a joint collaboration between task force members and research librarians (Appendix A1).

Figure 1 is a PRISMA flow diagram showing identification, screening, eligibility, and inclusion of articles. After initial review of the articles, studies prior to 2013 were excluded as not sufficiently up to date to reflect the current application of automated segmentation methodology. An additional search was performed using a second set of keywords (Appendix A2), resulting in an additional 226 studies. After removal of duplicates, a total of 7,770 citations were identified.

Each of the initial 7,770 citations was independently screened at the title/abstract level by two fellowship trained sub-specialty radiologists and/or experienced imaging researchers using predefined exclusion criteria: 1) animal, cadaver, or phantom studies, 2) radiation oncology studies, 3) dental studies, 4) studies using ultrasound, nuclear medicine, functional MRI, magnetic resonance spectroscopy, or diffusion tensor imaging, 5) studies using semi-automated or manual segmentation, 6) reviews and meta-analysis, 7) studies with fewer than 20 subjects.

After title/abstract screening, 1,771 articles were included in the full-text screening. Using the same exclusion criteria, an additional 923 articles were excluded. The remaining articles were divided by sub-specialty based on abstract keywords (neuroimaging, thoracic imaging, abdominal imaging, musculoskeletal imaging, breast, and adipose tissue imaging). At time of sub-specialty data extraction, 440 articles were excluded (Table 1). Studies excluded as outside the scope for this review were: studies of fetal or neonatal neurologic segmentation and studies of pathologic tissues or organs in thoracic and abdominal segmentation. Other exclusions were: free software (i.e., FreeSurfer, SPM, and FSL), commercial software (i.e., Neuroquant), or studies published in ArXiv for neurologic segmentation; non-human subjects, duplicate manuscripts, modality other than CT or MRI, non-English, reviews or meta-analyses, or use of commercial software for thoracic segmentation; duplicate studies for abdominal segmentation; cadaveric study, modality other than CT or MRI for musculoskeletal segmentation; duplicate or breast CT studies for breast segmentation. Following all exclusions, 408 articles were included in the systematic review.

### Methodological Quality

The methodological quality of 408 studies was assessed independently by two reviewers (LL and LH) according to a modified National Heart, Lung and Blood Institute (NHLBI) Case Series Quality Assessment Tool [19]. The NHLBI Quality Assessment Tool assesses study objectives, population, outcome measures, statistical method, and provides a Good, Fair, or Poor quality rating. Disagreements were resolved by consensus.

### Data Extraction

During full-text review, the following data were extracted: segmented organ or tissue, imaging modality, segmentation technique, sample size, and validation method. Because there is no single accepted classification method to describe segmentation methods, we applied a modified classification scheme, described by Withey and Koles [20]. The

segmentation techniques were divided into the following categories: 1) Thresholding, 2) Statistical, 3) Deformable model, 4) Graph search, 5) Multi-resolution, 6) Atlas-based, 7) Texture analysis, 8) Neural network, and 9) Hybrid (i.e., combination of more than one of the above methods) (Table 2).

## Results

408 studies met the inclusion criteria, including 145 (36%) neurologic, 78 (19%) thoracic, 87 (21%) abdominal, 58 (14%) musculoskeletal, 20 (5%) breast, and 20 (5%) adipose tissue studies. Using the NHLBI Quality Assessment Tool, all studies (100%) received a quality rating of Good.

### Neurologic Segmentation

145 studies met the inclusion criteria (Appendix B1). MRI was used in 137 (94%) studies, CT in 7 (5%) studies, and CT and MRI in 1 (1%) study. The MR field strengths were: 1.5T (n=31), 3T (n=34), both 1.5T and 3T (n=24), 1T (n=2), 7T (n=2), and not specified (n=45).

The most common pulse sequence for normal brain segmentations was 3D T1-weighted (n=56). For segmenting lesions in multiple sclerosis, gliomas, white matter hyperintense lesions, and stroke, FLAIR was combined with T1-weighted and/or proton-density and/or T2-weighted sequences (n=53).

The brain was segmented in 139 (96%) studies and the spinal cord in 6 (4%) studies. The brain structure most commonly segmented was the hippocampus (n=13). At the tissue level, techniques focused on segmenting lesions, gray matter, white matter, and cerebrospinal fluid. A few studies focused on other structures such as caudate, basal ganglia, thalami, individual gyri within a lobe, or brain stem.

A variety of automated segmentation techniques were used (Table 3). The most commonly used methods were statistical (n=59), atlas-based (n=38), and neural network (n=19). The number of subjects whose images were used for training and validation varied greatly across the studies (mean=218, range = 20–3672).

Most studies validated automated segmentation techniques against the ground truth determined by manual segmentation (n=102). Some techniques were validated against other established segmentation techniques (n=28). Finally, some validation used challenge datasets including Medical Image Computing and Computer Assisted Intervention (MICCAI), Brain Tumor Segmentation (BraTS), and the Alzheimer's Disease Neuroimaging Initiative (ADNI) (n=11). While many different validation metrics were used, the most common was the DSC (n=46).

Automated segmentation techniques were used in normal subjects as well as in subjects with various diseases or conditions including: Alzheimer's disease, multiple sclerosis, stroke, cancer, and epilepsy.

## Thoracic Segmentation

78 studies met the inclusion criteria (Appendix B2). CT was used in 30 (38%) of studies, MRI in 27 (35%), CT angiography (CTA) in 14 (18%), MR angiography (MRA) in 2 (3%). Five studies (6%) used a combination of modalities (e.g., CT and CTA).

Segmented organs included the heart (n=39), lungs and airways (n=19), and blood vessels (n=16). Four studies segmented multiple organs. Combinations included the heart and coronary arteries, heart and liver, heart and solid abdominal organs, and segmentation of all intrathoracic organs (i.e., skin, bones, and mediastinal structures).

All but one of the studies that segmented the lungs used CT (n=17). Most of the studies that segmented the blood vessels used CT or CTA (n=13). 62% of the studies that segmented the heart used MRI (n=24).

Cardiac segmentation typically isolated one or more cardiac chambers; most commonly, the left ventricle. Lung segmentation typically focused on isolating the lungs. A few studies segmented the individual lobes or the trachea and bronchial tree. Blood vessel segmentation typically focused on the coronary arteries, with some studies focusing on the great vessels.

A variety of automated segmentation techniques were used (Table 3). The most commonly used methods were deformable models (n=24), thresholding (n=19), and statistical (n=15). Most studies validated automated segmentation techniques against the ground truth determined by manual segmentation. In addition, 30% (n=25) of studies compared their method to previously published segmentation method. A small number of studies relied on visual comparison as their validation method; this technique was almost exclusively used to evaluate vascular segmentations. While many different validation metrics were used, the most common was the DSC (n=39).

The average number of exams used for training and validation varied widely across all studies (mean=151, range = 20–2500). Larger datasets were seen in studies using CT (mean=232) compared to those using MRI (mean=99). Even smaller datasets were seen in studies using CTA (mean=67) and MRA (mean=31).

Only a small number of studies used publicly available datasets, such as COPDgene, Lung Imaging Database, Cardiac Atlas Project Database, or the LIDC-IDRI database. Several studies used data from prior challenges, including the Rotterdam coronary CTA challenge, LOLA11 lung lobe segmentation challenge, and the 2012 MICCAI RV segmentation challenge.

Automated segmentation techniques were used in normal subjects as well as in subjects with various diseases or conditions including : cardiovascular diseases (e.g., coronary artery disease, prior myocardial infarction, ventricular hypertrophy, or congestive heart failure) and pulmonary diseases (e.g., chronic obstructive pulmonary disease or interstitial lung diseases).

## Abdominal Segmentation

87 studies met the inclusion criteria (Appendix B3). CT was used in 50 (57%) studies and included non-contrast and contrast-enhanced studies in various phases (i.e., arterial or portal venous). MRI was used in 36 (41%) studies and employed a variety of sequences including multiplanar T2- and T1-weighted pre- and post-contrast images. One study used both CT and MR images for multi-organ segmentation.

The organs segmented were: prostate (n=24), liver (n=20), kidneys (n=10), spleen (n=5), pancreas (n=5), colon (n=2), gallbladder (n=2), esophagus (n=2), bladder (n=1), and female pelvic floor (n=1). The remaining 15 studies segmented more than one organ; ranging from two organs (e.g., liver and spleen) to up to 14 distinct structures including the aorta, inferior vena cava, mesenteric vessels, and uterus.

A variety of automated segmentation techniques were used (Table 3). The most commonly used methods were atlas-based (n=19), deformable models (n=14), and neural networks (n=14). 17 studies used a combination of more than one method. Most studies (n=82) compared performance of the automated segmentation technique to manual segmentation. The average number of exams used for validation was 68 (range = 20–400). While many different validation metrics were used, the most common was the DSC (n=62).

## Musculoskeletal Segmentation

58 studies met the inclusion criteria (Appendix B4). CT was used in 20 (34%) studies, MRI in 37 (64%), and both CT and MRI in 1 (2%).

Segmentation of the spine was most common (n=16). Other segmented regions included: thigh/femur (n=13), pelvis/hip (n=10), knee (n=14), wrist (n=3), shoulder (n=2), lower leg (n=1), skull (n=1), and whole body (n=2). Five studies segmented multiple regions (e.g., femur and pelvis, spine and pelvis).

Bone was the most common tissue segmented (n=35). Additional segmented tissues included articular cartilage (n=14), fibrocartilage (n=3), skeletal muscles (n=9), intervertebral discs (n=4), bone-cartilage interface (n=1), spinal canal (n=1), and dural sac (n=1). Eight studies segmented more than one tissue.

A broad range of automated segmentation techniques were used (Table 3). The most commonly used methods were deformable models (n=13). Thirty studies used a combination of methods. Most studies compared performance of the automated segmentation technique to manual segmentation. The average number of exams used for training and validation was 170 (range = 20–2117). While many different validation metrics were used, the most common was the DSC (n=42).

Automated segmentation techniques were used in normal subjects as well as in subjects with various diseases or conditions including: osteoporosis, osteoarthritis, rheumatoid arthritis, avascular necrosis, fractures, meniscal injury, cancer, bone metastases, craniosynostosis, spinal stenosis, disc herniation, and disc degeneration. Some studies focused only on normal subjects.

## Breast Segmentation

20 studies met the inclusion criteria (Appendix B5). All studies used MRI. Sequences used for segmentation included axial non-fat-suppressed non-contrast T1-weighted images (n=8), multiple sequences (n=6), post-contrast T1-weighted or subtraction images (n=1), non-contrast T1-weighted fat suppressed (n=3), Dixon-based sequences (n=1), and sagittal non-fat-suppressed non-contrast T1-weighted images (n=1).

Most studies evaluated breast fibroglandular tissue (FGT) segmentation alone (n=11), with a subset extrapolating FGT segmentation to post-contrast images to evaluate background parenchymal enhancement (BPE) (n=3), or to evaluate FGT, BPE and lesion-level segmentation (n=6).

A broad range of automated segmentation techniques were used (Table 3). The most commonly used method was statistical (n=5). Eight studies used more than one method. Most studies compared automated segmentation to manually drawn contours as ground truth. The average number of exams used for training and validation was 90 (range = 20–400). The most common validation metric was the DSC (n=16).

## Adipose Tissue Segmentation

20 studies met the inclusion criteria (Appendix B6). CT was used in 12 (60%) and MRI in 8 (40%). The following examinations were used: abdominal CT (n=5), abdominal MRI (n=4), thoracic CT (n=8), thigh CT (n=1), thigh MRI (n=2), calf MRI (n=1), and whole body MRI (n=1). Two studies segmented multiple regions (e.g., abdomen and thorax, thigh and calf). Most studies performed segmentation of tissue volumes (n=17) rather than tissue cross-sectional area (n=3).

Abdominal visceral and subcutaneous adipose tissue were most commonly segmented (n=8), followed by epicardial or pericardial adipose tissue (n=7), thigh intermuscular adipose tissue and subcutaneous adipose tissue (n=2), and brown supraclavicular adipose tissue (n=1).

Atlas-based and deformable model techniques were used equally (Table 3). However, hybrid techniques were most common (n=12). In all studies, manual segmentations were used as the reference standard. The average number of exams used for training and validation was 100 (range = 20–530). The most common validation metric used was the DSC (n=13).

Automated segmentation techniques were used in normal subjects as well as in subjects with various diseases or conditions including: obesity, diabetes, metabolic syndrome, and osteoarthritis. Some studies focused only on normal subjects.

## Discussion

This is the first systematic review of automated segmentation that includes CT and MRI across all anatomic regions. The most significant finding of this review is that there is wide variability in approaches to automated segmentation, regardless of anatomic region or image modality. Another finding is that automated segmentation of the brain is far ahead of other organs and tissues. In fact, 79 studies on neuro-segmentation were excluded from our review



because they applied existing automated segmentation methods to clinical research, rather than developing new methods. Similarly, there were more studies of thoracic, abdominal, and musculoskeletal segmentation compared to breast and adipose tissue segmentation.

Our results should be interpreted in the context of prior literature on the three generations of medical image segmentation [20]. Fully automated methods often combine multiple segmentation operations and incorporate at least one second- or third-generation approach.

First-generation approaches use pixel intensities or connectedness to apply basic heuristics or one-time operations to segment the image. These include edge tracing (i.e., boundary segmentation) and thresholding and region growing (e.g., volume segmentation) [21].

Second-generation methods incorporate uncertainty models and optimization methods which typically avoid heuristics. These include approaches to segment volumes (i.e., statistical pattern recognition, c-means clustering), boundaries (i.e., deformable models), or other (i.e., graph search, neural networks, multiresolution methods) [20]. They commonly use classifiers for separating clusters, including k-nearest neighbors (k-NN), artificial neural networks (ANN), support vector machines (SVM), and random forest classifiers. Statistical pattern recognition is used to assign pixels a probability of belonging to a tissue class based on pixel intensity and/or texture classifiers (e.g., Bayesian, k-NN, maximum likelihood, expectation-maximization, Markov random field) [22–26]. In c-means clustering (including fuzzy c-means clustering), pixels are grouped into a known number of clusters based on pixel intensity or local texture by minimizing an objective function [22]. Deformable models (e.g., active contours, active surfaces, snakes, level-sets) can conform to image features over time under the influence of internal and external forces to achieve a local optimum [26]. Graph search techniques treat pixels as interconnected nodes in a graph, where graph cuts between the interconnected nodes are defined based on minimization of a cost function to produce a globally optimized segmentation [27]. ANNs learn from training data to classify pixels into predefined classes. In multiresolution segmentation, a high-to-low resolution image stack is created by iteratively blurring and down sampling the original image; pixels with similar features between the stacked images are linked as belonging to the same object to perform the segmentation [28].

Third-generation approaches incorporate higher-level knowledge such as *a priori* information, expert defined rules, and models of the shape or appearance of the target object, and include methods to segment volumes (e.g., atlas-based segmentation, rule-based segmentation) and/or boundaries (e.g., shape models, appearance models) [20]. Atlases of segmented images can be mapped to an unsegmented image, with the atlas supplying probabilities for statistical pattern recognition based on anatomical, shape, size, and textural features [29]. Segmentation can incorporate automated rule logic based on anatomy, intensity, texture, and/or shape [20]. Statistical shape models, such as the active shape model [30], are an extension of deformable models, where deformation is restricted by statistical bounds of the model. Active appearance models incorporate an “image patch” of shape plus intensity data into the statistical model to segment an object [31].

Despite this hierarchy, there is no consensus on how to categorize various segmentation methods. For example: Withey and Koles [20] categorize based on first-, second-, and third-generation; García-Lorenzo et al. [32] categorize based on supervised and unsupervised approaches; Danelakis et al. [33] categorize into: data-driven, feature-based, atlas-based, statistical, tissue-based, and lesion-based. For the purposes of our systematic review, we divided the segmentation techniques into: thresholding, statistical, deformable model, graph search, multi-resolution, atlas-based, texture, neural network, and hybrid. Our aim was to use a classification system that would be useful for readers who are new to the field.

Our review found a wide variability among automated segmentation methods: 1) statistical, atlas-based, and neural network methods were especially common in neuro-segmentation; 2) statistical, thresholding, and deformable model methods were most common in thoracic segmentation, 3) deformable model, atlas-based, and neural network methods were common in abdominal segmentation, and 4) hybrid models, employing a combination of techniques, were most common for musculoskeletal, breast, and adipose tissue segmentation. Although many different validation metrics were used to evaluate automated segmentation of various organs and tissues, the most common was the Dice similarity coefficient (DSC).

### Neuroimaging Segmentation

Segmentation of the brain and spine using MRI poses particular challenges owing to variability in acquisition parameters including slice thickness, resolution, matrix size, TR, and TE. To minimize this variability, preprocessing of images is critical. Preprocessing typically includes registration of images to a common template (i.e., Montreal Neurologic Institute) or co-registration of images, skull stripping, signal intensity normalization, noise reduction, and bias or field inhomogeneity correction [34].

In this systematic review, we did not discuss the advantages or disadvantages of various segmentation techniques as this is addressed in detail in prior narrative reviews [35]. It is difficult to compare different segmentation techniques as there is no consensus regarding optimal evaluation metrics or standardization of databases. This may be mitigated by the use of challenge datasets and development of guidelines for ML researchers [5].

Automated image segmentation relies increasingly on ML, including U-net and other convolutional neural networks [36,37]. However ML techniques require a large amount of annotated data for training, validation, and testing. Currently, there are not many large datasets that can be used to develop ML approaches to segmentation. Because there is heterogeneity in MRI protocols as well as differences in tissue contrast that vary with field-strength and MRI vendor, a segmentation technique for one MRI protocol may not be applicable for different protocols.

There have been two prior systematic reviews of segmentation using brain MRI [38,39] and one systematic review on using spine MRI [40]. Dicke et al. [38] performed a systematic review of brain MRI focusing on the creation of atlases for segmentation of normal brains and included 66 studies from October 2010 to August 2016. Cover et al. [39] performed a systematic review focused on segmentation of the corpus-callosum and included 36 studies prior to March 2016. Rak and Tonnies [40] performed a review of spine segmentation and 98

studies but did not follow the PRISMA guidelines. Our systematic review follows the PRISMA guidelines and includes 145 studies using MRI and CT of the brain and spine.

Unlike the systematic reviews that have been few in number, conventional narrative reviews of neuro-segmentation have increased dramatically. Between 2013 and 2018, there were 12 reviews of brain MRI [33,35,37,41–48], 3 of spinal cord MRI [49–51], 3 of brain CT [52–54], and 2 of spine CT [55,56]. While these reviews provide valuable information on neuro-segmentation techniques they do not provide the methodologic rigor of a systematic review and are subject to a selection bias.

### Thoracic Segmentation

This systematic review revealed multiple methods for automated segmentation of the organs of the thorax using CT and MRI. As expected, more methods used CT, which allows more accurate evaluation of the lungs and airways. However, more than half the studies of the heart used MRI. While 16 studies focused on vascular segmentation, only 6 evaluated the coronary arteries.

In a prior review of machine learning segmentation Slomka et al. [57] reported that most coronary segmentation methods require some manual initialization. Another review by Moccia et al. [58] reported that vascular segmentation requires a variety of approaches partly because there is no single approach for different types of vessels and that pathologic vessels may require different approaches than normal vessels.

The most commonly used automatic segmentation techniques that were identified in this review are generally the same as those identified in other published reviews. In particular, for segmentation of the heart on MRI, deformable models were the most common techniques [59]. Automated segmentation of the cardiac chambers is particularly challenging owing to normal or pathologic deformation of the heart during the cardiac cycle [60]. The field is very active, with many automated cardiac segmentation methods presented in recent conferences and on preprint websites that have not yet reached peer-reviewed journals [61].

The datasets used to evaluate automated segmentation methods in the thorax are relatively small. This is likely because the ground-truth used to evaluate these methods is resource-intensive and time-consuming to produce. Unlike in brain imaging, there are significantly fewer automated segmentation methods in the thorax that use public datasets.

Surprisingly, only 6% of the studies in our review used neural network approaches to automated segmentation in the thorax. Currently, these techniques are widely used for thoracic classification, but not segmentation. Since there is increasing number of studies using neural networks for pulmonary nodule segmentation [62,63], it is likely that the same methods will eventually be applied to other tissues in the thorax.

### Abdominal Segmentation

The development of automated segmentation techniques for abdominal and pelvic organs lags behind other body regions, especially the brain. The major challenges include: 1) variability in the shape, size and position of the anatomical structures of interest, 2) poor

contrast between adjacent organs and surrounding tissues (edge detection), 3) motion artifacts that can cause image blurring, and 4) change in organ position relative to other fixed anatomical structures [64].

Despite these challenges, an accurate approach to automated segmentation and measurements of abdominopelvic organs is highly desirable for many clinical indications. For example, accurate preoperative liver volumetry is becoming standard of care prior to major hepatic resection or for partial living donor transplantation [65]. Manual and semi-automated liver segmentation techniques are time-consuming and have high inter- and intra-reader variability. Accurate automated segmentation of kidneys is especially valuable when monitoring patients with autosomal dominant polycystic kidney disease [66]. Accurate segmentation of splenic volume aids in monitoring patients with infection and splenic diseases [67,68]. There are many other current clinical applications, including focal lesion detection in all abdominal organs, bowel segmentation for the detection of obstruction and inflammatory bowel disease, lymph node measurement, radiation treatment planning, and detection of aortoiliac atherosclerosis [12].

Common approaches to segmentation in abdominopelvic organs include detection of features, edges or intensities, strong or weak shape and/or location priors, thresholding, clustering methods, and deformable models with most automated segmentation techniques employing a combination of these techniques. Based on this systematic review, there are many automated segmentation techniques that can be applied to abdominal organs. However most of these have been validated in relatively small studies.

Direct comparison of the different approaches to automated segmentation is problematic as validation techniques vary from study to study. Challenges such as those sponsored by the MICCAI conferences and online publicly available datasets, will certainly foster the development of many more automated segmentation techniques for the abdomen.

### **Musculoskeletal Segmentation**

Studies of automated segmentation of bone commonly use CT, owing to the high image contrast between bone and soft tissue structures [69]. Studies using MRI are increasingly common for the evaluation of joints and soft tissues [70]. Although many studies use a combination of methods to automatically segment bone, the deformable model, atlas-based, statistical, and graph search methods are the typical components of these automated algorithms. Many approaches also incorporate first-generation segmentation methods such as thresholding, region growing, edge detection, and edge tracing into the segmentation framework.

Some studies have compared the performance of different segmentation methods in the same cohort of healthy and diseased subjects from public datasets such as SpineWeb [71]. Recent studies of six automated vertebral segmentation methods reported DSCs of 0.87–0.95 for normal spines and 0.54–0.90 for osteoporotic spines [72,73].

Studies that automatically segmented intervertebral discs most commonly use deformable models and statistical segmentation approaches. Recent segmentation competition challenge

reported on eight automated segmentation algorithms with DSC ranging from 0.82–0.92 [74].

Automated segmentation of musculoskeletal tissues has also benefited from ML. Neural networks [75] can now automatically segment joint tissues in approximately 5 seconds, while maintaining high DSCs.

The most common techniques used to segment cartilage and muscle include random forests, nearest neighbors, SVM, and k-mean clustering. When comparing different ML approaches, the results may vary based on study population. For MRI of muscle, Gadermayr et al. [76] reported that a basic thresholding approach was often sufficient, but shape based graph cuts produced the best results in patients with severe fatty infiltration of muscle. Many recent studies incorporate multiple models, such as combining localized classification via 2D and 3D convolutional neural networks (CNNs) with statistical anatomical knowledge via 3D statistical shape models [77].

Many studies have focused on automated articular cartilage segmentation on knee MRI using large publicly available datasets including the Osteoarthritis Initiative (OAI) and the MICCAI grand challenge “Segmentation of Knee Images 2010”. Recent studies used voxel-based relaxometry to obtain fully automated analysis of cartilage composition using T1-rho MRI [78]. Although early studies focused on only one anatomic structure (e.g., cartilage), it is increasingly common to segment multiple structures (e.g., bone, cartilage, meniscus). For example, a fully automated segmentation pipeline has been constructed for evaluation of both morphological and quantitative knee MRI data by combining a deep CNN and three dimensional (3D) simplex deformable modeling [79].

For skeletal muscle segmentation, most studies still use manual or semi-automated techniques, but this is beginning to change [80–84]. With MRI, one proposed strategy is automated quantification of whole-body muscle volumes. Karlsson et al. [81] developed an automated segmentation method based on multiatlas segmentation of intensity corrected water-fat separated image volumes, reporting high accuracy and reproducibility. Yang et al. [82] segmented muscle on a single image at the mid femur level (rather than tissue volumes), reporting shorter scan times and diminished post-processing computational costs.

The use of automated segmentation of muscle using CT is also increasing [11]. Lee et al. [82] used a deep learning system to automatically segment the muscle cross-sectional area of CT slices at the L3 vertebral body level, with an average of less than 3.7% difference between predicted and ground truth muscle cross-sectional area, while reducing segmentation time from 30 minutes to 0.17 seconds. Current challenges for automated segmentation of muscle using CT include a tendency to underestimate muscle area in general, while overestimating muscle area in subjects with edematous fat [83].

## Breast Segmentation

Breast segmentation on MRI consists of three separate challenges: 1) distinguishing breast-chest wall and breast-air boundaries, 2) separating breast FGT from fat, and 3) distinguishing abnormal breast enhancement from normal BPE.

There are unique challenges to breast segmentation that have limited large-scale application to date. Although Dixon-based sequences and other fat-specific sequences offer superior fat and glandular tissue segmentation, these are not routinely incorporated into most clinical breast MRI protocols. In comparison, T1-weighted pre- and post-contrast acquisitions are essential to diagnostic breast MRI but demonstrate B0 and B1 inhomogeneity across the parenchyma at the breast-air boundary and across the coil gradient [84]. Without appropriate correction of the varying enhancement caused by sources of inhomogeneity, image-processing methods can be inaccurate. Finally, the routine use of fat suppression can introduce additional artifact that must be corrected. Although breast MRI can be performed at both 1.5T and 3.0T, there is no evidence that segmentation differs between these field strengths.

There are two prior systematic reviews of breast segmentation. Wang et al. [85] reviewed breast and chest segmentation studies but did not include lesion-level automated segmentation studies or ML studies. Codari et al. [86] reviewed only ML studies. In contrast, our review includes fully automated breast segmentation examining FGT, BPE and lesion segmentation approaches.

In developing approaches for fully automated breast segmentation, hybrid approaches, incorporating both statistical and atlas-based methods are most common. For example, Wu et al. [87] used a fuzzy C means atlas-based method on sagittal T1W fat-suppressed imaging in 60 breast MRIs, achieving a Pearson correlation coefficient of  $r = 0.92$  for FGT% and a DSC of 0.67.. Similar template based approaches using fat-water separation have demonstrated high reliability for FGT separation [88,89]. However, fat-water separation techniques are not commonly used in routine clinical breast imaging. Statistical (particularly fuzzy c-means) and thresholding techniques have also shown promise in FGT segmentation. However, ML approaches will likely predominate in the future. Recent studies of SVM-based approaches and U-net approaches have resulted in higher DSCs and relatively fast processing times compared to more traditional approaches [90,91].

Lesion segmentation on breast MRI is particularly challenging. Deep learning techniques show the most promise in automatic lesion segmentation. Dalmi et al. [92] used a 2D U-net CNN to evaluate 361 cases using early post-contrast images to create a CADe system with a computation performance metric (CPM) of 0.6429, significantly higher than the CPM value of 0.5325 obtained by a previous CADe system utilizing a full dynamic breast MRI ( $p=0.008$ ).

### Strengths and Limitations

Our systematic review has several strengths and limitations. A major strength is that we used a comprehensive search strategy using three databases (PubMed, Embase, and Cochrane), yielding 7770 citations reviewed by sub-specialty experts using strict exclusion and inclusion criteria, resulting in 408 studies. Another strength is that we included organs and tissues of the entire body, rather than one region, and that we included both CT and MRI. One limitation is that we did not perform a meta-analysis to determine which automated method is most valuable. However, due to wide variability in the segmentation methods as well as the approaches to their validation, such meta-analysis is currently not feasible.

**Future Directions**—Future studies of automated image segmentation will undoubtedly involve methodological innovations as well as new clinical applications.

Most innovative methods at this time appear to involve deep learning (DL). DL is a subfield of machine learning (ML), which in turn is a subfield of artificial intelligence (AI). DL is based on artificial neural networks. Neural networks are machine learning devices modeled after the human brain. DL employs neural networks, consisting of layers of nonlinear processing units that successively process the numerical input data. A single processing unit (the artificial neuron) typically receives multiple inputs, combines them as a weighted sum, and applies to the results some form of a nonlinear transformation [93, 94]. Through training, the network learns the weights required to achieve its task [93, 94]. Especially well-suited to image analysis are the convolutional neural networks (CNNs). These networks use convolution kernels (i.e., filters) that are shared among all neurons in the same layer, drastically reducing the number of parameters in the network and allowing training with a relatively smaller number of datasets. CNNs have been successfully applied to image processing, segmentation, classification, and prediction [95]. U-net is a CNN that consists of encoding and decoding stages and is particularly well suited for image segmentation [96]. Recently, generative adversarial networks have also been gaining popularity [97, 98]. One major hurdle for further development of DL methods is the need for large datasets of annotated images for training. However, increasing availability of publicly available image databases such as ADNI, LONI, OASIS, should improve access to training images. Importantly, all DL methods require significant computational power. Increased availability of graphical processing units as well as open source frameworks such as Apache MXNet, PyTorch, Caffe, and Chainer has provided the needed computational resources to allow for increased application of DL methods to CT and MR image segmentation.

Future clinical applications of DL methods may include triaging patients with potentially life-threatening conditions or reducing common interpretive errors [12]. Future research applications will include large-scale integration of clinical, genomic, proteomic, metabolomic, and radiomic data as part of epidemiological studies as well as pragmatic trials [10].

## Conclusion

We conducted a systematic review that includes automated segmentation using CT and MRI of the entire body. Our findings have implications for both research and clinical practice. Automated CT and MR image segmentation allows for an objective evaluation of diseases by identifying quantitative imaging markers that are widely used in research. Major challenges to implementation of automated segmentation tools to clinical practice remain. For all the anatomic regions evaluated in our study, there is continuing need for further validation studies across different centers, scanner platforms, and acquisition parameters. Increasing use of machine learning approaches has accelerated the development of robust automated segmentation techniques. For this field to advance, it is imperative that radiologists who are the custodians of medical imaging data help create larger databases. More studies on larger populations are needed to validate automated segmentation techniques. Publicly available databases can provide access to large number of images. A list

of these databases can be found at (<https://wiki.cancerimagingarchive.net/display/Public/RIDER+NEURO+MRI>; [https://en.wikipedia.org/wiki/List\\_of\\_neuroscience\\_databases](https://en.wikipedia.org/wiki/List_of_neuroscience_databases); <http://www.aylward.org/notes/open-access-medical-image-repositories>). Eventually, automated segmentation techniques will be used in routine clinical practice to help improve patient care. Radiologists, biomedical engineers, and medical physicists will play a key role in transforming clinical radiology practice from being focused on qualitative image interpretation to a more objective quantitative identification of disease markers.

## Acknowledgments

### FUNDING

National Institute of Health: P30 AG021332 (LL).

## Appendix A1: Initial Search Strategy

(“Automatic”[tw] OR “Automated”[tw]) AND (((“Image Analysis”[tw] OR “Image Analytics”[tw]) OR (“Segmentation”[tw] OR “Segmentations”[tw]) OR (“Volumetric”[tw] OR “Volumetrics”[tw])) OR ((“Neural Networks”[tw] OR “Neural Network”[tw] OR “Neural Network Models”[tw] OR “Neural Network Model”[tw] OR “Connectionist Models”[tw] OR “Connectionist Model”[tw] OR “Perceptrons”[tw] OR “Perceptron”[tw] OR “Convolutional Neural Network”[tw] OR “Convolutional Neural Networks”[tw] OR “CNN”[tw] OR “CNNs”[tw]) OR (“Machine Learning”[tw]) OR (“Automated Pattern Recognition”[tw] OR “Pattern Recognition System”[tw] OR “Pattern Recognition Systems”[tw]) OR (“Computer-Assisted Image Processing”[tw] OR “Computer-Aided Image Processing”[tw] OR “Computer-Assisted Image Analysis”[tw] OR “Computer-Assisted Image Analyses”[tw] OR “Computer-Aided Image Analysis”[tw] OR “Computer-Generated Image Analysis”[tw] OR “Image Reconstruction”[tw] OR “Image Reconstructions”[tw]) OR (“Finite Element Analysis”[tw] OR “Finite Element Analyses”[tw] OR “Finite Element Method”[tw] OR “Finite Element Methods”[tw] OR “FEM”[tw]) OR (“Cluster Analysis”[tw] OR “Cluster Analyses”[tw] OR “Clustering”[tw] OR “Clusterings”[tw] OR “Disease Clustering”[tw]) OR (“Principal Component Analyses”[tw])) OR (“Neural Networks (Computer)”[majr:noexp] OR “Machine Learning”[majr:noexp] OR “Pattern Recognition, Automated”[majr:noexp] OR “Image Processing, Computer-Assisted”[majr:noexp] OR “Finite Element Analysis”[majr:noexp] OR “Cluster Analysis”[majr:noexp] OR “Principal Component Analysis”[majr:noexp])) AND (“Cardiac-Gated Imaging Techniques”[mesh:noexp] OR “Cardiac-Gated Imaging Techniques”[tw] OR “Radiographic Image Enhancement”[mesh:noexp] OR “Radiographic Image Enhancement”[tw] OR “Radiography, Dual-Energy Scanned Projection”[mesh:noexp] OR “Dual-Energy Scanned Projection Radiography”[tw] OR “Tomography, X-Ray Computed”[mesh:noexp] OR “X-Ray Computed Tomography”[tw] OR “Xray Computed Tomography”[tw] OR “Computed X-Ray Tomography”[tw] OR “X-Ray Computerized Tomography”[tw] OR “Computerized X-Ray Tomography”[tw] OR “CT X-Ray”[tw] OR “CT Xray”[tw] OR “CT X-Rays”[tw] OR “X-Ray CT Scan”[tw] OR “X-Ray CT Scans”[tw] OR “X-Ray Computer Assisted Tomography”[tw] OR “X-Ray Computer Aided Tomography”[tw] OR “X-Ray CAT Scan”[tw] OR “Transmission Computed Tomography”[tw] OR “Transmission CT”[tw] OR “Cine Computed Tomography”[tw] OR “Cine Computerized Tomography”[tw] OR “Cine CT”[tw])



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## Appendix A2: Secondary Search Strategy

(“tomography, x-ray computed”[MeSH Terms] OR (“tomography”[All Fields] AND “x-ray” [All Fields] AND “computed”[All Fields]) OR “x-ray computed tomography”[All Fields] OR (“computed”[All Fields] AND “tomography”[All Fields]) OR “computed tomography” [All Fields])) OR ((“magnetic resonance imaging”[MeSH Terms] OR (“magnetic”[All Fields] AND “resonance”[All Fields] AND “imaging”[All Fields]) OR “magnetic resonance imaging”[All Fields] OR “mri”[All Fields])) AND ((“tissue segmentation”[All fields] OR “tissue classification”[All fields] OR “machine learning”[All fields] OR “volumetry”[All fields] OR “neural networks”[All fields] OR “segmentation”[All fields]) AND (“automatic” [All Fields] OR “automated”[All Fields] OR “automatically”[All Fields]))

## Appendix B: Manuscripts Included in Systematic Review

### B1. Neurosegmentation

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## B2. Thoracic Segmentation

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### B3. Abdominal Segmentation

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## B4. Musculoskeletal Segmentation

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## B5. Breast Segmentation

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## B6. Adipose Tissue Segmentation

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## Abbreviations

|               |  |
|---------------|--|
| <b>ML</b>     | Machine Learning   |
| <b>DSC</b>    | Dice Similarity Coefficient                                |
| <b>MICCAI</b> | Medical Image Computing and Computer Assisted Intervention |
| <b>CNN</b>    | Convolutional Neural Network                               |
| <b>FGT</b>    | Fibroglandular Tissue                                      |
| <b>BPE</b>    | Background Parenchymal Enhancement                         |

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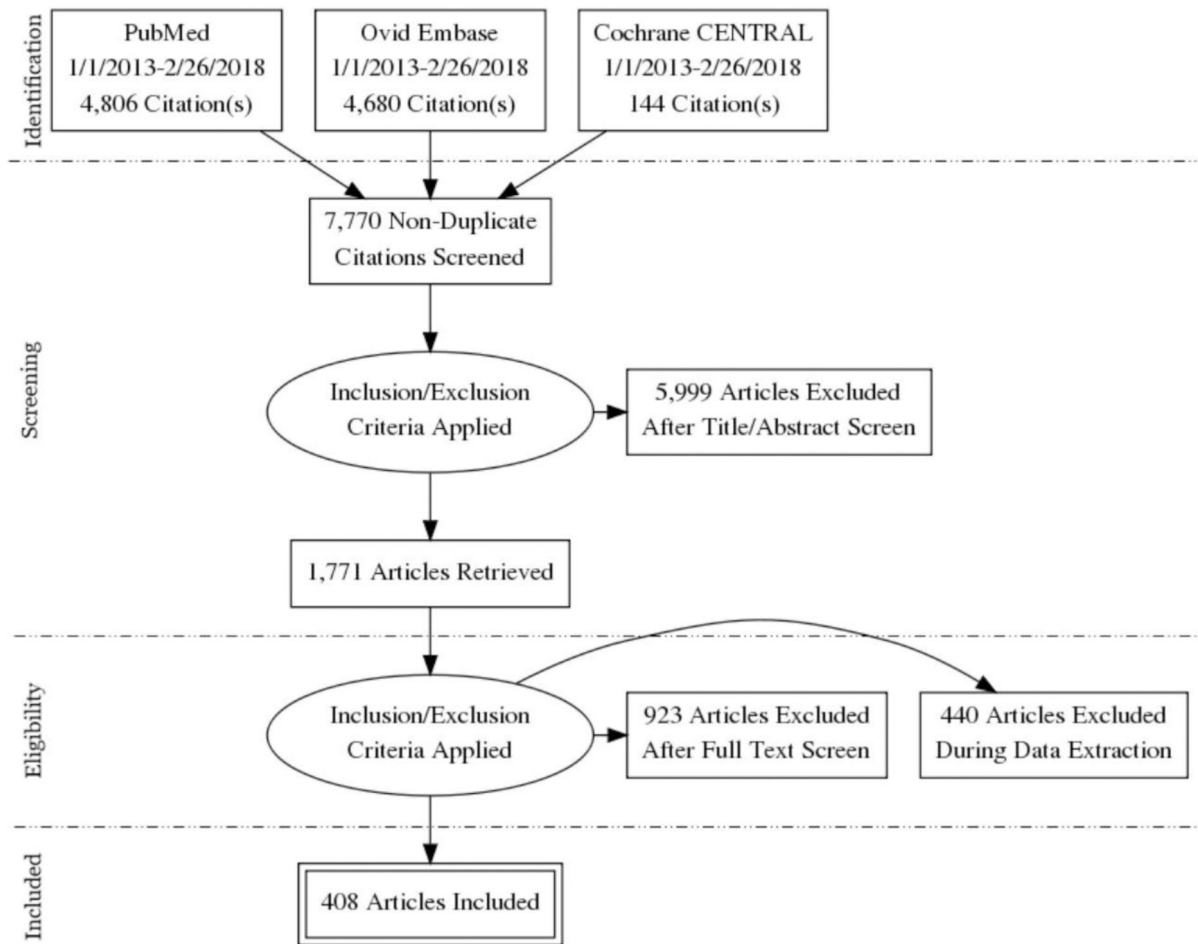
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**Figure 1:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram showing identification, screening, eligibility, and inclusion of articles.

**Table 1:**

Exclusions during sub-specialty review

| <b>Reason for Exclusion</b>                | <b>Neuro n=237</b> | <b>Thoracic n=67</b> | <b>Abd n=40</b> | <b>MSK n=63</b> | <b>Breast n=20</b> | <b>Adipose n=13</b> |
|--|--------------------|----------------------|-----------------|-----------------|--------------------|---------------------|
| Sample size < 20                           | 41                 | 26                   | 20              | 14              | 4                  | 7                   |
| Not fully automated                        | 5                  | 5                    | 6               | 7               | 1                  | 3                   |
| Classification without segmentation        | 0                  | 1                    | 3               | 7               | 4                  | 2                   |
| Insufficient detail on segmentation method | 10                 | 0                    | 1               | 9               | 0                  | 0                   |
| Application of existing methods            | 79                 | 0                    | 0               | 0               | 3                  | 0                   |
| Conference abstract                        | 58                 | 8                    | 0               | 14              | 5                  | 1                   |
| Full text not available                    | 5                  | 7                    | 1               | 6               | 0                  | 0                   |
| Outside the scope                          | 13                 | 4                    | 7               | 0               | 0                  | 0                   |
| Other exclusions                           | 26                 | 16                   | 2               | 6               | 3                  | 0                   |

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**Table 2:**

## Classification of segmentation methods

| Method           | Segmentation sub-categories  |
|------------------|--|
| Thresholding     | Intensity  |
|                  | Adaptive   |
| Statistical      | Statistical pattern recognition                                      |
|                  | Mixture model, k-nearest neighbor classifiers, Bayesian classifiers  |
|                  | Expectation-maximization, Markov random field, iterative procedure   |
|                  | Prior information modeling   |
|                  | C-means clustering, fuzzy c-means clustering, random forests         |
| Deformable model | Active contour, active surface, active shape, snake, level-set       |
|                  | Statistical shape  |
|                  | Appearance model   |
| Graph search     | Dynamic programming  |
|                  | Graph cut  |
|                  | Watershed  |
| Multi-resolution | Scale reduction  |
| Atlas-based      | Single atlas   |
|                  | Multi-atlas  |
| Texture analysis | Neighboring voxel relationships (intensity, gradient, entropy, etc.) |
| Neural network   | Convolutional neural networks (CNN)                                  |
|                  | Multi-class CNN  |
|                  | Multi-scale CNN  |
|                  | Visual geometry group (VGG)  |
|                  | Adversarial network  |
|                  | Deep learning  |
|                  | Deep belief network  |
| Hybrid           | More than one method listed above                                    |

**Table 3:**

Automated segmentation methods by anatomic region

| Segmentation Method                          | Neuro n=145 | Thoracic n=78 | Abd n=87 | MSK n=58 | Breast n=20 | Adipose n=20 |
|--|-------------|---------------|----------|----------|-------------|--------------|
| Thresholding                                 | 10          | 19            | 7        | 0        | 1           | 1            |
| Statistical                                  | 59          | 15            | 7        | 4        | 5           | 0            |
| Deformable model                             | 6           | 24            | 14       | 13       | 2           | 3            |
| Graph search                                 | 3           | 2             | 9        | 1        | 1           | 0            |
| Multi-resolution                             | 0           | 0             | 0        | 0        | 0           | 0            |
| Atlas-based                                  | 38          | 8             | 19       | 6        | 0           | 3            |
| Texture analysis                             | 6           | 7             | 0        | 0        | 0           | 0            |
| Neural network                               | 19          | 5             | 14       | 4        | 3           | 1            |
| Hybrid (combination of more than one method) | 6           | 8             | 17       | 30       | 8           | 12           |

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