Deep learning for quantitative cardiac MRI

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AJR FOCUS ON:

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OBJECTIVE. The recent advancement of deep learning techniques has profoundly impacted research on quantitative cardiac MRI analysis. The purpose of this article is to introduce the concept of deep learning, review its current applications on quantitative cardiac MRI, and discuss its limitations and challenges.

CONCLUSION. Deep learning has shown state-of-the-art performance on quantitative analysis of multiple cardiac MRI sequences and holds great promise for future use in clinical practice and scientific research.

Ever since the initial success of AlexNet (A. Krizhevsky) at the annual ImageNet competition in 2012 [1], deep learning methods have unleashed AlexNet's power and have swiftly swept through all areas of computer vision [2–4]. Medical image analysis, as a subfield of computer vision, has witnessed the same paradigm shift from traditional machine learning to deep learning [5, 6]. Cardiac MRI, the state-of-the-art imaging tool for evaluating the heart, benefits meanwhile ftrom the development of deep learning techniques to enhance its quantitative nature. This article aims to explain the concept of deep learning, review its current applications in quantitative cardiac MRI, and discuss its limitations for now and challenges for the near future.

The Concept of Deep Learning

The current popularity of deep learning in radiology calls for a clear explanation of its rationales to the radiologists. What is deep learning? Deep learning refers to the set of machine learning methods using multilayer neural networks (NNs) to analyze data [2]. The term "deep" comes from the fact that there are literally many layers of neurons—up to hundreds—between the input layer and output layer of a NN.

The concept of a multilayer NN [7, 8], initially conceived of to imitate the interconnection of neurons in the human brain [9], dates back to the 1950s. An NN performs mapping from input to output, and it learns the mapping from data: Given a set of input and output data, the NN uses a backpropagation algorithm [10] to learn the network parameters so that the input can go through these parameters to be mapped to the output. The deeper the network, the more complex a mapping it can learn. Once trained, the NN can be deployed—that is, it can perform the learned mapping on an unseen dataset. Despite its mathematic soundness, however, the utilization of NNs has been limited for decades because of a number of practical issues such as the tendency to overfit, the difficulty to converge, and a lack of computational power [3].

The late surge of deep learning can be attributed to the renaissance of the convolutional neural network (CNN), which facilitates raw image input and deep architecture [11–13], the development of advanced graphical processing units that enable fast computing, and the accumulation of a massive dataset that amplifies the concept of learning [14, 15]. Although the classic methods strive to first extract meaningful features from images (e.g., those representing edges, corners, lines, and so on) and to then classify these feature ensembles, deep learning methods integrate the two steps into one step: Deep learning methods simultaneously learn the feature representation and classification [2, 3] so that both are optimized by the data. Today, deep learning methods have shown excellent performance unmatched by classic machine learning methods in many areas of computer vision [4, 6].

Keywords: artificial intelligence, cardiac MRI, deep learning, quantitative MRI

doi.org/10.2214/AJR.19.21927

Received June 28, 2019; accepted without revision June 30, 2019.

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AJR 2020; 214:529–535

0361–803X/20/2143–529

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Cardiac MRI is an advanced and versatile cardiovascular imaging modality [16–18]. It is generally considered the reference standard method for evaluation of cardiac structure and function [19, 20]. Cardiac MRI is also widely used for myocardial scar assessment [21]. Recent mapping techniques further add to its quantitative nature: The myocardium can be characterized in absolute measures of milliseconds using T1 or T2 mapping or percentages using extracellular volume (ECV) quantification [22–25]. In addition, cardiac MRI is also used to quantify myocardial strain [26, 27] as well as intracardiac blood flow hemodynamics [28, 29]. Within one examination, cardiac MRI potentially delivers a rich spectrum of information covering cardiac structure, function, tissue, and flow, which greatly enhances our understanding of cardiac abnormalities in clinical diagnosis and scientific research.

To achieve this, however, each sequence demands quantification in its own way. Quantitative analysis for cardiac MRI has been a much loved topic in medical image analysis not only because of its clinical utility, but also because of its technical challenges [30–42]. The analysis methods need to tackle the vast variability in cardiac MRI data: the differences in abnormalities, morphology, size, and orientation of the heart and also differences in contrast, luminance, artifacts, FOV, and signal-to-noise ratio of the image data. Until the recent emergence of deep learning techniques, no classic image analysis method has shown sufficient promise to deal with such a combination of complexity and variability in clinical data. Thus, today's analysis of cardiac MRI still involves substantial manual input from radiologists; however, the situation is at the verge of change [43].

In the following sections, a brief review is given on the current deep learning research activities covering a wide spectrum of quantification analyses in cardiac MRI.

Structure Quantification

Cardiac MRI provides the reference standard measurement of cardiac structure, including thickness of the myocardial wall and end-systolic and end-diastolic volumes of the left ventricular (LV) and right ventricular (RV) cavities. The steady-state free precession (SSFP) cine sequence is commonly acquired in cardiac MRI examinations, but manually identifying the systolic and diastolic phases and annotating the frames (normally > 300 frames) is tedious and subjective. Automated algorithms for segmenting heart ventricles and blood cavities have been in development for decades; however, the last-generation algorithms are used mostly in the laboratory because it proved hard to reach the clinically acceptable accuracy and robustness necessary without considerable user interaction.

Multiple recent studies have suggested that deep learning methods using CNN may transform the situation [39, 44–47]. Initial studies in this direction used a pixel-classification CNN—for example, a CNN to classify if a pixel belongs to myocardium by evaluating its surrounding context (patches) [31, 48]. Later work adopted a more powerful network architecture called U-Net (O. Ronneberger, P. Fischer, T. Brox) [49], which is an end-to-end CNN. By learning from a high number of cine images with known LV and RV annotations, the CNN is able to formulate the complex mapping from the original cine image to its segmentation.

For clinical use outside the laboratory, however, it is important that the CNN trained on one particular dataset can generalize well to other datasets that were not seen during training. The dataset varied in published studies from a single dataset, to data for a big population, to multivendor and multicenter data [44–47]. With sufficient variability in the training set, a combination of accuracy, robustness, and generalizability could be reached without any user interaction, showing promise for eventually entering into regular clinical use [46]. In 2017, the first U.S. Food and Drug Administration–approved deep learning software product was launched for automated cine MRI segmentation [50], and studies are ongoing to validate its use in the clinic.

MR angiography (MRA) is an alternative for high-resolution 3D visualization of cardiac structures in situations in which a CT examination is not preferred [51, 52]. Deep learning methods again showed outstanding performance in segmenting complex cardiac anatomies from MRA images (e.g., segmenting left atrium [LA] with pulmonary veins [PVs] in patients with congenital heart disease) [53–56]. For the MRA images with nearly isotropic resolution, studies showed that a 3D variant of U-Net can take better advantage of the rich imaging content and can achieve even higher performance than the original 2D U-Net [53–56].

Function Quantification

From a segmented cine MRI examination, cardiac function parameters, including left ventricular ejection fraction (LVEF) and right ventricular ejection fraction, are readily derived. Interesting technical development have been made beyond the U-Net, which in its original form processes each cine frame separately. Notwithstanding its good performance, such a CNN sees cine MRI in a way very different from human experts: It analyzes each frame separately, whereas radiologists tend to view the frames in cine mode and pay attention to the cardiac motion. Deep learning CNN can be designed to imitate the behavior of an experienced radiologist. In a recent work [57], an extra module of optical flow [58] was integrated into the U-Net so that the motion between frames could be extracted to enhance the temporal coherence of segmentation. The optical-flow U-Net showed further improved segmentation performance over the original U-Net—in particular, at challenging locations such as base and apex where individual segmentation often goes awry. This work exemplifies how deep learning methods can integrate human experience on a higher cognitive level.

Another interesting technical development is a deep CNN that maps the original cine MRI directly to all structural and functional parameters without intermediate LV and RV segmentation [59]. The CNN architecture consists of an image autoencoder network that extracts the low-dimensional features from the cine MRI study and a regression network that makes quantitative predictions from these features. The two networks are jointly optimized by the training data. This data-to-parameter approach showed the strong capability of deep learning methods to perform highly nonlinear and complex mapping defined by the user.

Strain and Motion Quantification

Function measurements (e.g., LVEF) are frequently used in clinical practice for guiding cardiovascular disease treatment; however, they can be insensitive to early remodelling of the heart [60, 61]. Changes of mechanical properties in local myocardial muscles may occur before global manifestation of function impairment [20, 61]. Myocardial strain, defined as the rate of myocardial tissue contraction or relaxation, is widely used for quantification of the mechanical properties of myocardium.

Cardiac MRI provides several possibilities to quantify regional myocardial strain. Specific pulse sequences, such as tagging and displacement encoding with stimulated echoes (DENSE), can be used to assess myocardial deformation. Use of these sequences in the clinic is, however, limited because of the need for an extra acquisition and the complexity of image postprocessing. Myocardial deformation can also potentially be extracted from a regularly acquired SSFP cine sequence. The feature tracking (FT) method similar to that for speckle echocardiography can be used; however, FT cardiac MRI lacks a firm physical ground because there are no random patterns (e.g., speckles) in cine MRI as there are in echocardiography [61].

Deep learning methods can go beyond semantic segmentation of cine MRI to further address the analysis of cardiac motion and thereby strain in the myocardium. In a recent work [62], a deep learning CNN was designed to analyze the unenhanced cine images of patients with chronic infarction and to produce a map of infarction based on the local motion extracted from the network. The cine-based infarction map showed good agreement with infarction localization derived from late gadolinium-enhanced (LGE) MRI, with a sensitivity of 90% and specificity of 99%. The work shows the possibility of identifying myocardial scar by motion analysis without administration of a contrast agent. Although myocardial strain was not explicitly addressed in this work, it can be extracted as an intermediate output from the CNN. Research works in this direction are in fast development [57, 63, 64], and clinical validation is warranted to prove the value of CNNs in the clinic.

Tissue Quantification

A unique strength of cardiac MRI is its capability to noninvasively assess myocardial tissue properties. LGE MRI is the reference standard technique for assessment of myocardial scar [16, 21] and has significant diagnostic and prognostic value for a range of cardiovascular diseases [65–68]. Accurate segmentation and quantification of LGE MRI are also highly relevant for advanced studies such as interventional procedure guidance and individualized risk stratification [69–72]. In the medical literature, there are two established LGE MRI quantification methods—namely, the SD method and the full width at half-maximum (FWHM) method [72–74]. Both methods require manual input from the observer: first the myocardium region and then the ROI of infarcted or remote myocardium region need to be manually annotated. The SD method defines a threshold of the annotated remote myocardium as follows:

$$\text{mean} + N \times SD,$$

where mean is the mean signal intensity in the annotated healthy myocardium region, N is the coefficient that ranges from 1 to 7, and SD is the SD of signal intensity in the annotated healthy myocardium region. The FWHM method defines a threshold as a percentage of the maximum signal intensity in the annotated infarcted myocardium (P) (e.g., 50%). Myocardial regions with signal intensity higher than this threshold are recognized as scar. The two methods are widely adopted; however, it has been difficult to reach a consensus value of N or P in spite of earnest search in multiple studies [74–76]. The right numbers are subject to the image noise level, scar pattern, ROI size, and MRI sequence parameters, all of which vary among patients, centers, vendors, and observers.

The problem of data-specific parameters can potentially be addressed by deep learning CNNs, which "see" enough annotated LGE images to infer the image-to-segmentation mapping. In [77], a patch-based CNN was developed to classify myocardial scar in patients with a history of infarction. In [78], an end-to-end U-Net architecture was adopted to simultaneously segment the LV myocardium and scar from the LGE MR images of patients with a history of infarction. The methods were extended to a more complicated scenario, the segmentation of atrial scar on LA and PVs [79, 80], the morphologies of which are highly irregular and variable. Initial work has shown state-of-the-art accuracy of LA and PV segmentation and reasonable accuracy of scar segmentation [79]. Once clinically validated, the deep learning method can have important clinical implications for atrial fibrillation treatment and management. Atrial scar extent is considered to be an important prognostic factor for patients with atrial fibrillation, and accurate scar delineation facilitates the interventional procedure and potentially improves its efficiency and efficacy [81, 82].

An important development in cardiac MRI is the recent development of parametric mapping techniques, including T1, T2, T2*, and ECV techniques [22–25, 83]. The mapping sequences can be used to detect diffuse cardiomyopathies in the absence of focal scar and to identify subclinical myocardial involvement before structural or functional remodelling [83, 84]. Quantitative tissue mapping enables studies to be performed across different centers, vendors, and longitudinal time points. To report the myocardial T1, T2, T2*, and ECV values, however, radiologists need to perform manual annotation of the myocardium and blood pool against the varying contrast. A recent study [85] showed that ROI identification can be automated by deep learning methods so that quantification of myocardial T1, blood T1, and ECV can be accomplished automatically. In the same spirit as cine image segmentation, a deep learning CNN was trained to segment the myocardium and blood region given a large set of annotated T1-weighted frames. The CNN achieved fast performance (< 0.3 second per image) with high accuracy (Dice index = 0.85). The method further reported T1 values highly correlated to those obtained from manual annotation, with an intraclass correlation coefficient comparable to that between two expert readers [85]. This work again shows the high capability of CNNs to learn from data because T1 mapping sequences further a strong complication in addition to the existing cardiac MRI variability: At a different inversion time, the image contrast changes drastically because of gadolinium dynamics. The robustness of the CNN to contrast variability implies that the same rationale can be applied to T2, T2*, ECV, and perfusion images for automated reporting.

Other Developments

In previous sections, a number of research works have been reviewed, most of which involved segmentation of cardiac structures. Cardiac segmentation is a basis for further quantification, and parameters of cardiac structure, function, strain, and tissue can be derived from it. Importantly, segmentation of cardiac structures also enables visual check and manual editing whenever necessary, providing an important means of interaction to the users.

Technical developments have been made beyond cardiac segmentation. Deep learning networks can be trained to reconstruct high-quality cardiac MR images from seriously undersampled (up to 9 times) k-space data [86]. This capability implies the possibility of substantially accelerated cardiac MRI acquisitions in the future. Learning-based methods were also developed to perform quality control for cardiac MRI acquisition, to detect incomplete or corrupted

images [87], and interestingly to control the quality of automated segmentation [88]. Experiments on the large UK Biobank database [89] showed the feasibility to automate quality control steps that are conventionally performed by expert observers.

Deep learning research has also extended to clinical diagnosis. In 2017, a technical challenge was organized by a medical imaging society [39] with the dual goal of heart segmentation and disease classification; that is, based on a cine MRI acquisition, the goal was to classify a heart into one of five classes: normal, heart failure, dilated cardiomyopathy, hypertrophic cardiomyopathy, and abnormal right ventricle. Not surprisingly, deep learning methods achieved the best performance, and an accuracy of 96% was reported for fully automated diagnosis [90]. In the same light, a more recent work developed a dedicated CNN to learn the motion between cine frames and synthesized the shape and motion features to classify cardiac abnormalities [64]. Deep learning further shows the capability to predict survival in population studies. Bello et al. [63] developed a deep learning network named 4Dsurvival to predict subject survival in 12 years on the basis of cardiac motion extracted from cine MRI. The 4Dsurvival network reported higher predictive accuracy than the human benchmark (Harrell C-index, 0.75 vs 0.59).

This article has highlighted a number of interesting developments in quantitative cardiac MRI using deep learning techniques and does not intend to be complete; the field remains young and fast evolving. Exciting new developments are being made and to be expected.

Discussion

Implications for Clinical Practice and Scientific Research

To date, deep learning has found many successful applications in quantitative cardiac MRI. Existing studies show the unprecedented capability of deep learning methods to automatically process the complex multisequence cardiac MRI data and produce clinically relevant quantitative measurements. When extensively and thoroughly validated, deep learning methods will further empower cardiac MRI, the unique tool for cardiac imaging.

Deep learning can be the radiologists' aid for reading cardiac MRI examinations. Cardiac MRI typically is a lengthy examination, in terms of both acquisition and reporting. Even for experienced radiologists, it takes more than 15 minutes to report a cardiac MRI study. The quantification of LVEF alone, for example, involves exhaustive visual inspection and manual annotation. Deep learning may speed up this process: It can provide segmentation and quantification in a few seconds for almost all sequences of cardiac MRI, and the radiologist may only need a few minutes to inspect the intermediate segmentation and to approve the results. Because the fatigue of manual analysis is taken away, radiologists can focus on more patient-oriented issues such as history and diagnosis. By automating cardiac MRI reading, deep learning can also allow cardiac MRI to be offered at more centers with radiologists with less experience or centers with a high volume of patients and not enough radiologists.

The integration of deep learning with cardiac MRI has significant implications for scientific research. Deep learning opens new possibilities for cardiac MRI quantification. For example, the difficulty of atrial scar analysis (either manually or automatically) has been a bottleneck to further develop and validate the clinical concepts related to scar in management of atrial fibrillation. Accurate, objective, automated atrial scar segmentation by deep learning can play an important role in future research in this direction. Population studies such as the UK Biobank [89], in which tens of thousands of participants are recruited, can also benefit from deep learning. Whereas manual analysis for tens of thousands of cardiac MRI data was practically impossible in the past, deep learning can handle them now in a batch and can yield valuable quantitative parameters for generating and testing hypotheses. Meanwhile, the improved accuracy, precision, and objectivity of deep learning have positive effects on clinical trials that use cardiac MRI to monitor treatment effects. Increased precision in quantification, when incorporated into the power calculation, implies that fewer participants are needed. The staffing requirements from core laboratories can also be reduced with deep learning tools that are always precise and never weary. Both can reduce the cost of these typically expensive trials.

Limitations and Future Directions

Deep learning started to be an important concept in radiology not long ago. Debate on its future role in radiology is still ongoing. To fully embrace deep learning and tap its power, it is important to recognize its advantages as well as its limitations.

From a theoretic point of view, deep learning is a statistical method that learns only the statistics of the training dataset. It can work extremely well on the training set, thanks to its capability to learn arbitrarily complex mapping, and it can also generalize well to a testing dataset with identical or similar statistical distributions. However, given a testing dataset with different statistical distributions (e.g., different MRI device and different patient cohort), it can fail in an unexpected way. The scarcity of publically available cardiac MRI data with annotation also contributes to the difficulty and uncertainty for a deep learning model to generalize. For clinical use of the developed deep learning tools, therefore, it is very important that they go through rigorous multivendor and multicenter validation. Even so, close supervision from radiologists remains necessary.

A common criticism on deep learning is its black-box nature. A deep learning CNN can contain millions of parameters (neuron connections) that are simultaneously optimized by the backpropagation algorithm, but their contributions to the final results are beyond interpretation or control. A prominent research area, adversarial learning, actually shows that by adding carefully calculated, visually indiscernible disturbances to the input, one can make the CNN produce arbitrarily wrong output (e.g., the famous gibbon-panda example). The possibility of abuse of deep learning–based systems—especially in a clinical scenario, at the cost of patients and radiologists—is alarming. Interpretability and controllability are essential for clinical use; deep learning systems with intermediate output such as segmentation that can be visually inspected and edited are preferred over a complete black box that only produces a quantitative report.

Deep learning does not equal deep thinking, as its name may imply; instead, it can be superficial because it is dogmatic, faithful only to data. When the data are biased, the deep learning algorithm is biased. Deep learning systems are also inferior to human vision because the black box is much more susceptible to adversarial attacks than humans are. Higher-level thinking, generalization, and cognition in presence of disturbances are exactly what radiologists are trained on and good at. To combine the merits of machines and humans in future work would bring the most benefits to patients, clinicians, and health care systems.

Deep learning for quantitative cardiac MRI is not merely a technical problem; it is ultimately a clinical problem. Thus, in

future work, the use of deep learning to define and solve clinically relevant problems is essential. For example, deep learning can extract an accurate map of infarction from cine MRI in patients with chronic infarction, but the same concept may not apply to patients without a history of ischemia. Likewise, a deep learning CNN may be able to accurately delineate ischemic scar from LGE MRI, but it may encounter difficulties when the scar pattern changes to be subepicardial, patchy, or diffused as can occur in patients with nonischemic cardiomyopathy. Future deep learning research on quantitative cardiac MRI calls for close collaboration between computer scientists, radiologists, cardiologists, and MRI physicists.

Conclusion

Deep learning is state-of-the-art for automated quantitative cardiac MRI analysis. It has shown excellent performance on multiple cardiac MRI sequences and shows great promise for clinical use. Deep learning algorithms can provide useful information to the radiologists and will enhance the value of cardiac MRI in clinical practice and scientific research. Meanwhile, research effort should be devoted to further improve its generalizability, interpretability, and controllability.

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