Separation of water and fat signal in whole-body gradient echo scans using convolutional neural networks

Running title: Water and fat separation using neural networks

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Abstract

**Purpose:** To perform and evaluate water and fat signal separation of whole-body gradient echo scans using convolutional neural networks.

**Methods:** Whole-body gradient echo scans of 240 subjects, each consisting of five bipolar echoes, were used. Reference fat fraction maps were created using a conventional method. Convolutional neural networks, more specifically 2D U-nets, were trained using 5-fold cross-validation with one or several echoes as input, using the squared difference between the output and the reference fat fraction maps as the loss function. The outputs of the networks were assessed by the loss function, measured liver fat fractions, and visually. Training was performed using a GPU. Inference was performed both using the GPU as well as a CPU.

**Results:** The final loss of the validation data decreased when using more echoes as input, and the loss curves indicated convergence. The liver fat fractions could be estimated using only one echo, but results were improved by use of more echoes. Visual assessment found the quality of the outputs of the networks to be similar to the reference even when using only one echo, with slight improvements when using more echoes. Training a network took at most 28.6 h. Inference time of a whole-body scan took at most 3.7 s using the GPU and 5.8 min using the CPU.

**Conclusion:** It is possible to perform water and fat signal separation of whole-body gradient echo scans using convolutional neural networks. Separation was possible using only one echo, although using more echoes improved the results.

**Keywords:** magnetic resonance imaging; water-fat separation; Dixon; neural network; deep learning; convolutional neural network
Introduction

The vast majority of the signal in $^1$H MRI of humans without implants originate from either water or fat molecules. It is often of interest, both in clinical practice and in research studies, to separate the water and the fat signal from each other. For certain types of scans, this can be performed in post-processing by utilizing the property of chemical shift, which was first proposed by Dixon in 1984 (1).

The methods used for water and fat signal separation have since been refined. The most important addition has been taking the amplitude of the static magnetic field ($B_0$) inhomogeneity into account, without which the signal separation will be incomplete (2). The inclusion of the effective transverse relaxation rate ($R_2^*$) and a multi-peak fat spectrum results in an even more complete signal separation (3).

After signal separation it is possible to calculate the percentage of the total signal originating from fat, the so called fat fraction, which is a useful quantitative measurement. As an example, the fat fraction of the liver can be used to evaluate hepatic steatosis, thereby avoiding biopsies (4).

To perform the signal separation, at least two echoes are needed, or else the problem is underdetermined. However, a few methods have been developed to perform the signal separation using a single echo by making assumptions of the composition of the voxels (5, 6). The assumptions can lead to severe errors where they are not valid, which is probably the main reason why these methods are not commonly used.

The signal separation can be performed using either gradient or spin echoes. When using a normal Cartesian k-space trajectory, the gradient echo sequences will produce echoes of two different polarities. Using only echoes of one polarity avoids the problems associated with signal separation of bipolar echoes. Echoes of opposing polarities will have the water-fat signal shift in opposite directions and might have a small difference in the signal strength. Additionally, polarity dependent phase errors induced by eddy currents have to be taken into account when three or more bipolar echoes are used (7, 8).

Recently a class of machine learning algorithms called artificial neural networks, often shortened to neural networks or even just networks, have become extremely popular, especially within image processing. This is due to their often excellent performance compared to other machine learning algorithms. Today virtually all neural networks contain multiple hidden layers, and therefore fall under...
the category deep learning. Within image processing, so called convolutional neural networks are commonly used (9).

Neural networks have been used within MR image reconstruction to transform data from k-space to image-space (10, 11), calculate parametric maps in MRI fingerprinting (12), and recent conference abstracts show promise in water and fat signal separation (13–16).

In this paper, a method for separation of water and fat signal in whole-body gradient echo images is presented and evaluated. The method builds upon a previous conference abstract (13). Separation is performed using both a single echo as well as multiple echoes.

## Methods

### Source data

Whole-body imaging data from the POEM study (17), where all subjects are 50 years old, was used. In this paper a total of 240 scans, each of a different subject, were included after removal of scans of poor quality. Poor quality included excessive motion artifacts and errors in the scanning protocol, minor metal artifacts were accepted. Approval of the POEM study was obtained from the regional ethics committee, and each participant gave their written informed consent.

The images were all acquired on a 1.5T clinical scanner (Achieva; Philips Healthcare, Best, The Netherlands). A three-dimensional spoiled gradient echo sequence was used. A total of five bipolar echoes were collected. The following parameters were used: voxel size = 2.07 x 2.07 x 8 mm³ (sagittal x coronal x axial), Tₑ₁ = 1.37 ms, ΔTₑ = 0.95 ms, TR in range: 6.65–7.17 ms, and flip angle = 3°. The images were collected with continuously moving bed imaging (18), resulting in several subvolumes. The whole-body images were of size 256 x 184 x 252 voxels.

### Reference method

The three monopolar echoes were used to create reference signal separation with the previously described analytical graph-cut method (19), producing water and fat images, as well as fat fraction, R₂*, and field maps. One subvolume was processed at a time. Due to noise and model imperfections the fat fraction maps could contain values lower than 0% or higher than 100%, these values were set to 0% and 100% respectively.

### Neural networks
Modified versions of the U-net (20), which is a type of convolutional neural network, were used in this paper. They were trained to calculate the fat fraction of axial slices, using different number of echoes as input.

The U-net is described in detail in the original paper (20), but will be described in brief here. An input image will go through convolutions, producing multiple features, after which the features are downsampled to a lower resolution. This process is repeated a few times. After this the resulting features goes through some more convolutions and the resulting features are then upsampled, after which a concatenation with the previous features of the same resolution is performed using so called skip connections. This process is repeated until features are produced of the same resolution as the original input image. Finally, some more convolutions are perform to produce the output. A visual representation of a modified U-net used in this paper can be seen in Figure 1.

Figure 1. A visual representation of one of the networks used in this manuscript, with an axial slice containing the real and the imaginary parts of one echo as input and the corresponding fat fraction image as output. The cyan boxes represent feature maps. The white boxes represent feature maps that have been transferred by the skip connections. The horizontal numbers represent the number of features in a layer and the vertical numbers represent the number of elements per feature of the layer.

The networks used in this paper were implemented in TensorFlow 1.8.0 (21), and were based on the implementation used in (22). Differences compared to the original implementation in (20) will be described, but the implementations are otherwise identical.
The networks were trained using different configurations of the available echoes as input. Networks were either trained with echoes of both polarities or only echoes of one polarity, i.e. only odd or only even numbered echoes. For the three different sets of echoes used, all possible configurations using the first available echo and different numbers of consecutive echoes were used. Using echoes of both polarities explores if and how much this might improve the resulting separation.

As input one 2D axial slice with channels corresponding to the real and the imaginary parts of the echoes was used. The input was zero-padded to be of size 256 x 256. The input was scaled to be within the range -1 to 1, with 0 representing no signal.

The original implementation of the U-net would return an output that was smaller than the input, i.e. the result would be cropped, due to the convolutions. This was not desirable for the current problem, and was rectified by performing reflective paddings inside the networks after the convolutions, which made the output the same size as the input.

The implemented networks had one feature map as output. As loss function the voxelwise squared difference between the reference fat fraction, scaled to the range 0 to 1, and the output was used. This implies that the networks were trained to calculate fat fraction maps. Background voxels were excluded when calculating the loss function since they contain only noise and could potentially interfere with the training of the networks. Background was defined slicewise using Otsu's threshold (23) on the sum of the reference water and fat images. Slices containing only background were semi-automatically identified and excluded.

The networks were trained using a 5-fold cross-validation, split at the subject level, i.e. 80% of all subjects were used for training and 20% for validation, and this was repeated 5 times so that all data was used in the validation. The split was randomized. All slices of the training sets were used to perform training one at a time in a random order. One pass over all these slices is known as one epoch. The Adam optimizer (24) was used to train the networks. The following parameters were used: initial learning rate: 0.001, $\beta_1 = 0.9$, $\beta_2 = 0.999$, $\varepsilon = 1e-8$. The learning rate was decayed by a factor 0.8727 after each epoch.

The networks were trained for 16 epochs. After each epoch every second slice that was used for validation and every eighth slice that was used for training were run through the network to calculate loss curves.

**Water and fat signal images**
Water and fat signal images can be created from the resultant fat fraction maps of the trained networks. The signal of the echoes of spoiled gradient echo sequences can be described as:

\[ S_n = (W + a_n F) e^{i\omega_0 + (i\omega - R_2^*) t_n} \]  \[1\]

Where \( S_n \) is the signal at echo time \( t_n \), \( W \) and \( F \) are the magnitudes of the water respectively the fat signals, \( \omega_0 \) describe the initial phase of the signal, \( \omega \) the off-resonance shift, and \( R_2^* \) is the effective transverse relaxation rate. \( a_n \) is:

\[ a_n = \sum_{m=1}^{M} \alpha_m e^{i \gamma B_0 \delta_m t_n} \]  \[2\]

Where \( \alpha_m \) are the relative magnitudes of the \( M \) different fat peaks and \( \delta_m \) are their corresponding chemical shifts relative to water. Values were adapted from (25). \( B_0 \) is the amplitude of the static magnetic field and \( \gamma \) the gyromagnetic ratio of \( ^1H \).

If the fat fraction (FF) is defined as \( F/(W+F) \), and \( R_2^* \) assumed to be zero, it is possible to calculate \( W \) and \( F \) as:

\[ W = \left| \frac{S_n(1-FF)}{1+FF(a_n-1)} \right| \]  \[3\]

and

\[ F = \left| \frac{S_n^{FF}}{1+FF(a_n-1)} \right| \]  \[4\]

In case multiple echoes were used, \( W \) and \( F \) can be calculated as the average for the different echoes to improve the signal-to-noise ratio.

**Hardware**

All networks were trained using a GPU of type GeForce GTX 1080 Ti. Furthermore, inference was performed using both the GPU as well as a CPU of type Intel Xeon W-2102.

**Evaluation**

The final values of the loss function for the subjects used for validation is a measure of how well the networks performed. In addition to this the quality of the outputs of the networks were assessed by measured liver fat fractions and visual inspection.
To perform the measures of the liver fat fraction the livers were manually segmented. The fat fractions of the livers were calculated as the median of all voxels that were segmented. The performances of the different networks were evaluated by calculating the mean absolute error. Furthermore, it was evaluated how well the networks classified the fat fractions of the livers as normal or abnormal/fatty, using the commonly used cut-off value of 5.56\% (4).

Visual evaluation consisted of searching for errors in the images inferred by the networks, as well as finding qualitative differences compared to the reference images.

The time taken to train the networks with different number of echoes were measured, including the time taken to produce the loss curves. Inference time was also measured.

Results

All results will refer to the output of the fully trained neural networks with validation data as input unless otherwise stated.

Loss function

In Figure 2 the loss curves for the networks using echoes of both polarities are shown. It can be seen that after a few epochs the curves for the validation data flattens out, even though the curves for the training data continues to decrease. This indicates that no overfitting has taken place, and that the output of the networks converged for the validation data.
Figure 2. Curves showing loss per foreground voxel for the networks using echoes of both polarities. Dashed lines are used for training data, solid lines for validation data.

In Table 1 the final loss per foreground voxel of the validation data for all the different configurations of echoes used are shown.

**Table 1.** Final loss per foreground voxel of the validation data.

| up to echo # | 1     | 2     | 3     | 4     | 5     |
|-------------|-------|-------|-------|-------|-------|
| all echoes  | 0.0187| 0.0126| 0.0066| 0.0054| 0.0022|
| odd echoes  | 0.0187| -     | 0.0069| -     | 0.0022|
| even echoes | -     | 0.0165| -     | 0.0113| -     |

Liver fat content

When evaluating the networks ability to calculate the liver fat fractions it was noticed that the scans of two subject was faulty, probably due to errors in the scanning protocol, and they are not included in the
results regarding the livers, leaving 238 subjects. In Figure 3 the liver fat fractions estimated by the neural networks using echoes of both polarities are plotted against the reference fat fraction. It can be seen that even when using only one echo it is possible to estimate the liver fat fractions. The estimates improve with more echoes, and are almost identical to the reference when using all five echoes.

![Graph showing liver fat fractions estimated by the neural networks using echoes of both polarities plotted against the reference fat fraction.](image)

**Figure 3.** Liver fat fractions estimated by the neural networks using echoes of both polarities plotted against the reference.

According to the reference fat fraction, the liver fat fraction was normal for 214 of the subjects and abnormal for the remaining 24. Table 2 shows the mean absolute error of the liver fat fraction calculated using the neural networks, and Table 3 shows the number of misclassified livers. Both tables make it clear that by using more echoes the results improved.

**Table 2.** Mean absolute error of the liver fat fraction calculated using the neural networks.

| up to echo # | 1   | 2   | 3   | 4   | 5   |
|--------------|-----|-----|-----|-----|-----|
| all echoes   | 1.71| 1.18| 0.69| 0.39| 0.03|
| odd echoes   | 1.71| -   | 0.93| -   | 0.04|
| even echoes  | -   | 1.52| -   | 1.22| -   |
Table 3. Numbers of livers misclassified as normal/fatty.

| Up to echo # | 1  | 2  | 3  | 4  | 5  |
|--------------|----|----|----|----|----|
| All echoes   | 6/2| 1/0| 1/0| 0/0| 0/0|
| Odd echoes   | 6/2|   | 5/1|   | 0/0|
| Even echoes  |   | 5/1|   | 0/0|   |

Visual inspection

In Figure 4 axial fat fraction images of the abdomen, including the liver, of a subject with a fatty liver is shown. Both the reference fat fraction map and the fat fraction maps inferred by the networks using echoes of both polarities as input are shown. Two improvements are noticeable when increasing the number of echoes used. Firstly, the images get crisper, and secondly, the fat fraction of the liver gets closer to the reference. When using all five echoes, the inferred image is almost identical to the reference. The images are representative, with exception for the high liver fat.
**Figure 4.** Axial fat fraction maps of the abdomen of a subject with a fatty liver (reference fat fraction 12.28%). Background has been removed from all images for clarity. **a–e.** Results using neural networks. 

- **a.** Using the 1st echo,  
- **b.** using the 1st and the 2nd echoes,  
- **c.** using the 1st through the 3rd echoes,  
- **d.** using the 1st through the 4th echoes,  
- **e.** using all 5 echoes.  

**f.** Reference.

In Figure 5 coronal water signal images of a subject are shown. The image to the left was created using a neural network with the first echo as input, and the image to the right is the reference. The image created using the neural network is very similar to the reference, using more echoes improves the results slightly (not shown since the differences are very slight). However, there are some minor differences between the two images, mainly visible in the intestines and at the interface between the subvolumes, which can be identified by the horizontal strikes. Selected images are representative.
Figure 5. Coronal water signal images of a subject. a. Image created using a neural network with the first echo as input. b. Reference.

In general, visual inspection found that the quality of the inferred images was close to that of the references. As exemplified in Figure 4, using only a few echoes often lead to a visibly erroneous liver fat fraction in subjects with an abnormally high liver fat fraction. Other than this, errors were rare. Small but noticeable errors not present in the reference were found in the subcutaneous adipose tissue of two subjects with an abnormal amount of subcutaneous adipose tissue. These errors did not completely disappear with more echoes, but became less pronounced. Errors near some metal implants were more noticeable compared to the reference when using few echoes, although this discrepancy disappeared
when using more echoes. Finally, water-fat swaps were relatively common in the arms in the reference images, probably due to being in an inhomogeneous area of the main magnetic field, and also present in the anterior subcutaneous adipose tissue of the abdomen in a few subjects, possibly due to motion. These two problems were less pronounced in the images inferred by the neural networks, even when only using one echo as input.

Run time

The time taken to train a network was 15.4h for 1 echo, 17.2h for 2 echoes, 20.2h for 3 echoes, 24.8h for 4 echoes, and 28.6h for 5 echoes. Using the GPU, inference per slice took 12 ms when using 1 echo, rising to 15 ms when using 5 echoes, corresponding to 3.0 s respectively 3.7 s per whole-body scan. When using the CPU, inference per slice took 1.4 s, corresponding to 5.8 min per whole-body scan, regardless of the number of echoes used.

Discussion

In this study it has been shown that separation of water and fat signal in whole-body gradient echo images is possible using convolutional neural networks. Separation was possible using only a single echo, even though this is an underdetermined problem, although the results, especially the quantitative measurements, improved when using more echoes, with near identical results to a reference method when provided the same input. The possibility to perform signal separation using only a single echo allows for quicker scanning, which could be useful in situations where a fast scan time is critical.

In this study, only the fat fraction maps were directly inferred using the neural networks, and the water and the fat signals were calculated using these. Tests (not shown) appear to indicate that part of the difference between the calculated water images and the reference is due to this extra calculation step. If the networks had been trained to directly infer the water and the fat signals the differences with the reference method could potentially be reduced.

The networks could have been trained to produce $R_2^*$ and field maps. In the case of $R_2^*$ this was not attempted since the reference $R_2^*$ maps were of very poor quality, presumably since the MRI protocol used was not optimized for this. Field maps were not produced since they very seldom are of interest, but this could be a subject of future study.
It was found that using echoes of both polarities improved the results somewhat, compared to discarding echoes of either polarity. The difference was noteworthy for at least one of the measures in tables 1–3 when using echoes up to #4. The difference between using all echoes of both polarities or only all odd echoes was negligible. This is potentially due to the reference separation having been calculated using only the odd echoes. Using the two first odd echoes resulted in a smaller loss and mean absolute error of the liver fat fraction than using the two even echoes. This despite the even echoes having far more advantageous echo times than the first two odd echoes, as can be calculated using Cramér-Rao bounds. Again, this might be due to the odd echoes having been used for calculating the reference separation. However, using the two first odd echoes resulted in less misclassified livers than using the two even echoes, this might however have been a coincidence. In contrast, using only the second echo provided better results than using only the first echo.

In this study versions of the 2D U-net were used. The downsampling steps of the networks allow them to get a greater perceptive field, while the skip connections allow them to preserve fine details. The perceptive field is necessary to prevent water-fat swaps, and especially crucial when using only one echo as input since there otherwise would be impossible to find a good solution. Using a 3D architecture would extend the perceptive field into an additional dimension, and could potentially improve the results. However, this could lead to an increase in the time needed to perform training.

A GPU is needed to train the networks in a reasonable time, since the training of a single network would likely have taken upwards to a month or more using the CPU. Once trained however, the inference time is reasonable even when using a CPU.

One general drawback of neural networks is that there is no guarantee that they will generalize to other datasets. Obviously, the trained networks used in this study cannot accept more than five echoes. Furthermore, input containing data differing too much from that used during training could cause problems. For example data collected using a different protocol or type of scanner or of subjects belonging to a different age group or with pathology not seen during training. A future study could for example train a network with input from multiple studies or use synthetic data to attempt to overcome this problem.

In this study, errors were observed in the subcutaneous adipose tissue of two subjects with an abnormal amount of subcutaneous adipose tissue. This could potentially be due to a lack of this phenotype in the training data. The training data could potentially be expanded by augmentation in an attempt to
circumvent this problem. If this was to be attempted, it could be important to make sure that the augmentations are realistic, otherwise the networks might just take longer time to train, without any improvement in performance.

It is unclear how the networks with only one echo as input manage to calculate the fat fraction. A human observer can often determine the tissue type from magnitude images, and in this way give a rouge estimate of the fat fraction for each voxel. Furthermore, it is possible to take into account that there are correlations between obesity and fat fraction values. It is likely that the networks utilize similar approaches. Tests (not presented) showed that it was possible to calculate fat fraction estimates using only the magnitude images as input, although results were less accurate than when using complex images. This indicates that the networks were able to take the phase into account. This could be done for example by estimating the contribution to the phase from imperfections in the hardware and then taking the magnetic susceptibility of the different tissues/air into account, and in this manner model the fat fraction.

Conclusions

It has been shown that it is possible to separate the water and the fat signals of whole-body gradient echo scans using neural networks. Interestingly, separation was possible using only one echo, although using more echoes improved the results.

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