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Quantitative Experimental Phantom Study Based on Abdominal MR Contrast Media Using Deep Learning

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This study provides data for the development of oral contrast media for abdominal magnetic resonance imaging (MRI) examinations for potential use in clinical practice. The signal intensities, signal-to-noise ratio (SNR), and contrast-to-noise ratio (CNR) were quantified using various contrast media with longitudinal (T1) and transverse relaxation (T2) pulse sequences. Prediction accuracy error comparisons were conducted according to the mean-squared, mean-absolute, and root-mean-squared errors of the contrast media intensities using the Orange data mining software. The signal strength and SNR were higher in canola oil and pineapple juice (T1-weighted images), -while the intensities of blueberry juice and apple juice were high in the T2-weighted images; SNR was high in blueberry and cranberry juice, and CNR was high in Solotop® and blueberry syrup. The accuracy of the deep-learning prediction errors of MR signal intensities was high. In conclusion, data from ex vivo MRI research can be used for the development of oral contrast media.

Keywords : contrast-to-noise ratio, contrast media, deep learning, oral magnetic resonance imaging, signal-to-noise ratio

1. Introduction

The development of fast imaging sequences that provide the ability to acquire motion-free longitudinal (T1)- and transverse (T2)-weighted images of fluids from magnetic resonance (MR) scans have led to increased interest in MR imaging (MRI) of the digestive tract, providing important information about disease progression [1]. Irrespective of this pulse sequence choice, collapsed intestines can prevent the detection of lesions; therefore, luminal dilatation is a necessary prerequisite for small intestine imaging methods. It is thus necessary to study the usefulness of various orally administered contrast media in phantoms.

MRI is an imaging technique that uses a superconducting magnet and radiofrequency (RF) electromagnetic waves to acquire anatomical and physiological information about the human body based on the resonance responses of proton atoms in the subject's body [2].

Oral contrast media, such as using Gastrografin® and barium sulfate, are used in computed tomography (CT) and fluoroscopy in clinical abdominal examinations to increase the diagnostic rate of diseases and the boundary between the digestive system and surrounding tissues.

In MR examinations, if the image of the target area is not clearly visible or it is impossible to identify lesions for various reasons, the examination is conducted using orally administered or intravenous injections of contrast media. Several MR oral contrast media with different signal properties are classified as positive or negative. Positive contrast media decrease the T1 relaxation time and thus increase the signal intensity of the intestinal lumen [1]. Negative contrast media typically use superparamagnetic particles that induce inhomogeneities, thus shortening both the T1 and T2 relaxation times.

Oral negative contrast media are used for MR cholangiopancreatographic (MRCP) imaging. Negative contrast media lower the signal value of the target tissue and blood vessels, thus lowering the signal value of the gastrointestinal tract and increasing the signal value of the pancreatic duct hidden by the gastrointestinal tract, making it easier to observe pancreatic lesions [3].

An ideal contrast media used in magnetic resonance imaging should be nontoxic, have no adverse effects on patients, and should be evenly distributed within the target tissue [4]. New, low-cost, oral contrast media that

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satisfy these conditions and are less burdensome to the patient are drawing attention as ideal contrast media as they are based on fruit [5]. Optimal oral contrast media should have the following characteristics: they must maintain a stable contrast while they pass through the small intestine, have no intestinal absorption, and be completely excreted through the gastrointestinal tract. They should be well tolerated by patients in terms of taste, amount of intake, and timing of oral administration, and should be inexpensive. Finally, they should be safe, and should not cause allergic reactions or adverse effects [1].

In this study, oral and chemical contrast media were used and tested to identify the optimal conditions for use as MR oral contrast medias. The purpose of this study was to identify a new oral contrast media based on experimental phantom tests, generate basic data from its use for future development and application in clinical practice.

2. Contrast Media and Signal Intensity

The evaluation of digestive organs using MRI depends on the use of oral contrast media. The contrast media have good digestibility, uniform distribution in the intestinal lumen, exhibit no changes in contrast when diluted throughout the gastrointestinal tract, and are nontoxic. They are ideal for MRI if induce no peristaltic stimulation and if they have an acceptable cost [6].

Oral contrast media are commercially available but are accompanied by possible adverse effects. As shown in Table 1, oral contrast media are generally classified into positive-contrast media, which increase the signal of the digestive system, and negative-contrast media, which decrease the signal of the digestive tract. Their effects on signal intensity were quantified.

Various contrast methods are available for MRI. Negative-contrast media yield low-signal intensities on both T1- and T2-weighted images, whereas positive-contrast media yield high-signal intensities; biphasic-contrast media yield low-signal intensities in T2- and T1-weighted images [7]. Fluid contrast media are mainly used in both males and females for MRI intestinal motility recordings.

According to the physics of MRI, the signal intensity of MR oral contrast media is related to the integral of the proton spin density [N(H)], T1, and T2. These three parameters can be determined using a simplified signal intensity (SI) equation in the case of a spin-echo sequence [8].

$$SI = N(H) \times e^{(-TR/T1)} \times [1 - e^{(-TE/T2)}] \quad (1)$$

2.1. Positive contrast media

MR-positive contrast media decrease the T1 relaxation time, thereby increasing the lumen signal intensity in the intestines. The concentrations used clinically have little or no effect on the T2 relaxation time; thus, high signal intensity is exhibited even on T2-weighted images owing to the water content of the contrast media. Theoretically, the higher the concentration is, the higher the T2 effect is; this effect is manifested by signal loss on T2-weighted images.

Table 1. Classification of diversity of oral and chemical MR contrast media, signal intensity, solutions and descriptions [1].

Contrast media	Solution	Descriptions
Negative contrast	Pineapple juice (100 %)	Fruit juices may act as negative oral contrast media if the manganese concentrations are very high
	Apple juice (10 %)	
	Orange juice (10 %)	
	Grape juice (10 %)	
	Cranberry juice (27 %)	
	Blueberry juice (10 %)	
	Prune juice (100 %)	
	Blueberry syrup (10 %)	
	Solotop®	Barium sulfate acts like water
Positive contrast	Canola oil (100 %)	Longitudinal relaxation (T1)-weighted images increase the signal intensity, reduce T1 relaxation time, brighten lumen
Contrast	Water	Least expensive, safest, and most available contrast media
Chemical contrast	Gastrografin®	A water-soluble iodinated radiopaque contrast media. Each mL contains approximately 367 mg organically bound iodine
	Iodinated contrast media	Hexosure® solution used for injection at 755 mg (350 mg I)/mL

Other natural substances, such as milk, vegetable oil, ice cream, green tea, and blueberry juice can act as MR-positive contrast media because they can shorten the T1 relaxation time [6]. The rationale for making blueberry juice a positive-contrast media is its high content of manganese, a metal ion characterized by a high-magnetic moment that can shorten T1. Regardless of the manganese concentration, there is also a T2 negative effect depending on the shortening of the T2 relaxation time [9, 10].

In addition, because of their fat content, milk, vegetable oil, and ice cream have inherently short T1 values, thus yielding increased signals on T1-weighted images, whereas green tea has been found to produce high signals on T1-weighted MRI [11]. A commercial positive-contrast media applied to the digestive system is Magnevist® enteral (gadopentetate dimeglumine; Schering Healthcare Limited, Burgess Hill, United Kingdom) [12].

2.2. Negative-contrast media

MR negative-contrast media are generally used for MRCP and the gastrointestinal tract to reduce high-signal intensities; blueberry, pineapple, and date syrup are indicative examples.

MR negative-contrast media typically consist of superparamagnetic particles that act by inducing local magnetic field inhomogeneities, thus shortening both the T1 and T2 relaxation times. When a superparamagnetic contrast media is used, the T2-weighted effect is dominant; accordingly, the T2 effect caused by the dephasing spin results in a loss of signal intensity in the T2-weighted image and yields a low-signal intensity in the T1-weighted image [8,13]. In MRCP, pineapple juice was used as a negative-contrast media in a study in which image quality was often degraded by high signals in the gastrointestinal tract [14].

Perflubron (perfluorooctyl bromide, Imagent® GI, Alliance Pharmaceuticals, San Diego, CA, USA), which is a commercially available negative contrast media that yields dark digestive tract lumen on T1- and T2-weighted images [15], Lumirem (ferumoxsil oral suspension; Laboratoire Guerbet, Anulnay-sous-Bios, France) [16], and the superparamagnetic iron oxide (SPIO) MR contrast media ferristene (Abdoscan; Nycomed Amersham, Oslo, Norway) [17] have been used clinically.

2.3. Water

As an MR oral contrast media, water is the cheapest, safest, and most extensively used oral contrast media. It does not allow ideal distension of the distal ileum in most patients, and although intestinal absorption is the main limitation, it does not allow distension of the small intestine during digestion [18]. Therefore, water has been used with various additives to reduce intestinal absorption [19]. Therefore, this study compared and analyzed the signal intensities of water with those of other contrast media in MRI.

2.4. Barium sulfate

The signal intensity of barium sulfate depends on the degree of dilution; its signal intensity is low in T1-weighted images and varies from media to high in T2-weighted images. Barium sulfate can be used as a negative-contrast media because high concentrations produce low signal intensities in both T1- and T2-weighted images. At various concentrations, barium sulfate behaves like water. The main advantages of barium sulfate are its low cost, safety, and worldwide commercial availability, while its disadvantage is its long transit time, which increases inspection time [19, 20].

2.5. Manganese

Positive contrast media in the digestive tract increase the signal in the lumen by shortening or having an essentially short T1 due to the paramagnetic effects in nearby tissues; these agents are usually based on heavy metal ions, such as gadolinium, manganese, iron, and copper [21].

Manganese is used as a positive-contrast media because of the paramagnetic effects of manganese ions; it also has a T2 effect manifested by the shortening of T2 regardless of its concentration. Manganese hydrochloride (Lumenhance, Bracco, Milan, Italy) is a manganese-containing contrast media that is minimally absorbed in the small intestine upon entering it, thus increasing the signal intensity on T1-weighted images and decreasing the signal intensity on T2-weighted images. Therefore, it has been used as a biphasic agent [1, 22].

3. Materials and Methods

3.1. MR scanning

For the experimental study of abdominal MRI scans, a 3.0 T MR scanner (Ingenia, Philips Healthcare, Best, The Netherlands) was used, as shown in Fig. 1. The coil used for the MR scan was an 8-channel surface coil, and the images were compared and analyzed in the Picture Archiving and Communication System Image Viewer (MicroDicom; version 2022.3, MicroDicom, Sofia, Bulgaria) by scanning with T1 and T2 pulse sequences using various imaging acquisition parameters.

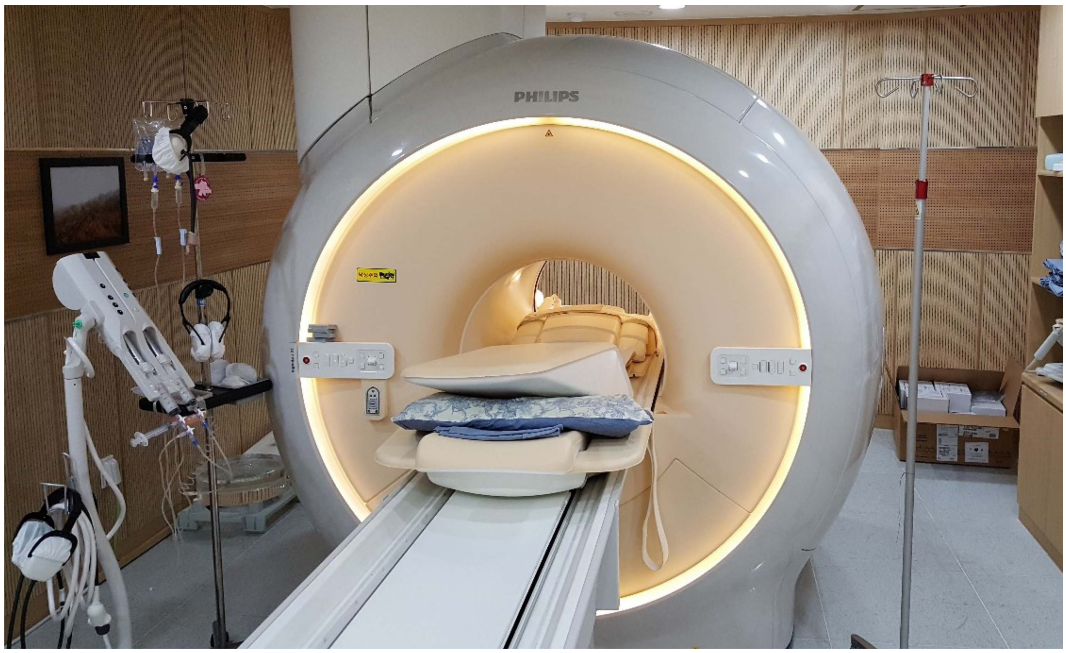


Fig. 1. (Color online) Magnetic resonance image acquisitions were conducted in the Philips Healthcare 3.0 T Ingenia system using the contrast media phantom.

3.2. Contrast media

The contrast media used in the MR scans were selected from available oral and chemical contrast media and were used in an experimental phantom study. As listed in Table 2, the oral contrast media used were water, 100 % Sweetio pineapple juice (Dole Food Co., Inc., Westlake Village, CA, USA), 10 % apple juice (Del Monte, Seoul, Korea), 10 % orange juice (Del Monte, Seoul, Korea), 10 % grape juice (Del Monte, Seoul, Korea), 27 % cranberry classic juice (Ocean Spray, UK), 10% blueberry juice (Woongjin Food Co., Ltd, Seoul, Korea), 100 % prune juice (Carson International Co., Ltd., Carson, CA, USA), 100 % canola oil (Dongwon, Seoul Korea), and 10 % blueberry syrup (Great Northern Maple Products Inc., Saint-Honore-De-Shenley, Quebec, Canada). Other chemical contrast media used in the MR phantom study were barium sulfate suspension (Solotop®, Taejoon Pharmaceuticals, Seoul, Korea), meglumine amidotrizoate (Gastrografin®; Bayer AG, Leverkusen, Germany), and the intravenous iodinated contrast media of iohexol (Hexosure 350®, Pharvis Korea, Seoul, Korea) (Fig. 2).

Table 2. Concentrations of different oral and chemical contrast media used in the experimental phantom study.

Contrast media (concentration)	Manufacture	Energy (kcal)	Fat (g)	Protein (g)
Pineapple juice (100 %)	Dole	500/1000 mL	0.6 (1 %)	1
Apple juice (10 %)	Del Monte	60/190 mL		
Orange juice (10 %)	Del Monte	60/190 mL		
Grape juice (10 %)	Del Monte			
Cranberry juice (27 %)	Ocean Spray	155/340 mL	0	0
Blueberry juice (10 %)	Woongjin	135/200 mL	0	0
Prune juice (100 %)	Carson International	655/946 mL	0	8
Canola oil (100 %)	Dongwon	900/100 g	100 (196 %)	0
Blueberry syrup (10 %)	Great Northern Maple Products Inc.	210/250 mL	0	0
Solotop®	Taejoon Pharmaceuticals			
Hexosure®	Pharvis Korea			
Gastrografin®	Bayer AG			

Fig. 2. (Color online) Photograph of different MR oral and chemical contrast media used in the experimental phantom study.

Table 3. Magnetic resonance pulse sequence parameters of T1 weighted images using the oral and chemical MR contrast media.

Parameter	Details
Repetition time (TR) (ms)	450
Echo time (TE) (ms)	9.58
Echo train length (ETL)	1
FOV (mm)	100
Slice thickness (mm)	5.0
Number of excitations (NEX)	1
Matrix	480 × 480
Flip angle (°)	70

Table 4. Magnetic resonance pulse sequence parameters of T2-weighted images using the oral and chemical MR contrast media.

Parameter	Details
TR (ms)	3000
TE (ms)	80
ETL	16
FOV (mm)	100
Slice thickness (mm)	5.0
NEX	1
Matrix	480 × 480
Flip angle (°)	90

3.3. MRI-based calculations

Fruit juice and chemical contrast media were dispensed into a 10 mL syringe with the needle removed. Water, pineapple juice, apple juice, orange juice, grape juice, cranberry juice, blueberry juice, prune juice, oil, blueberry syrup, Solotop®, Gastrografin®, and iodinated contrast media (Hexosure®) were prepared by filling 10 mL syringes in order. The prepared contrast media were arranged in the MRI device to obtain MR signal values.

A surface coil was used in the experiment, and a single-pass imaging acquisition of the contrast media was conducted to obtain T1-weighted images. The imaging parameters were: TR = 450 ms, TE = 9.58 ms, echo train length (ETL) = 1, field-of-view (FOV) = 100 mm, slice thickness (ST) = 5 mm, number of excitations (NEX) = 1, acquisition matrix = 480 × 480, and flip angle = 70° (Table 3). To obtain T2-weighted images, the parameters were adjusted and a single-pass imaging acquisition was also conducted. The imaging parameters were: TR = 3000 ms, TE = 80 ms, ETL = 16, 100 mm FOV, ST = 5.0 mm, NEX = 1, matrix = 448 × 256, flip angle = 90° (Table 4).

The signal intensity and background of the different contrast media in T1- and T2-weighted images were calculated, as shown in Fig. 3. The size of the region-of-interest (ROI) for measuring the signal intensity of tissue and signal intensity outside the tissue was set to 60 mm^2 and measured five times to calculate the average and standard deviation (SD).

To compare the signal strength, the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) were measured. The SNR was obtained by dividing the signal strength in the tissue by the background noise [23]; SNR is an index used to evaluate image quality. Based on this, the suitability of fruit juices as oral contrast media was determined.

$$SNR = S/\sigma \quad (2)$$

where S is the signal intensity in the set ROI with the contrast media, and σ is the SD value of a background ROI. CNR is the contrast-to-noise ratio that can be obtained by dividing the signals of different contrast media by the SD (which is the noise); CNR is used as an

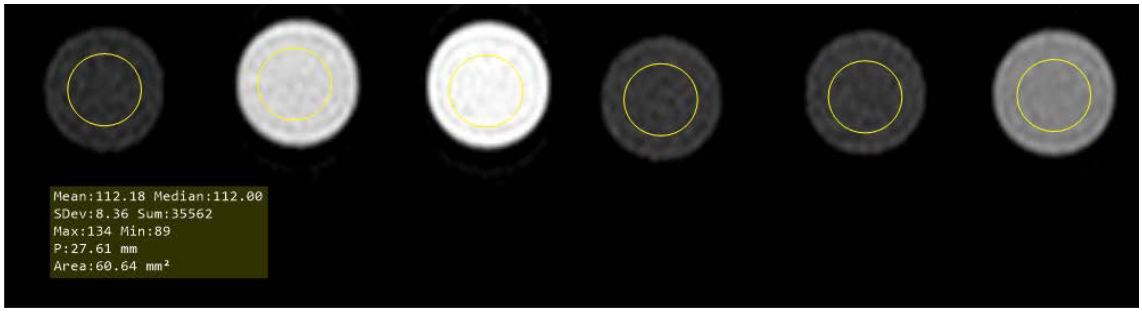


Fig. 3. (Color online) Axial longitudinal relaxation (T1)-weighted MR images of contrast media (left to right) water, iodinated contrast media, pineapple juice, apple juice, orange juice, and grape juice, and mean and standard deviation measurements using the region-of-interest (ROI) function of the MicroDicom Viewer.

index to evaluate the relative image quality. In this experiment, the CNR value of the contrast media was measured using water.

$$CNR = (S_1 - S_2)/\sigma \quad (3)$$

where S_1 and S_2 are the signal strengths of the contrast media in the phantom and σ is the SD of the background.

3.4. Deep learning

Statistical analyses focus on the identification of risk factors for disease, and machine learning prevents disease by focusing on the prediction accuracy of the probability of disease occurrence based on these risk factors. Research in deep learning is active in MR and medical imaging [24].

The mean-squared error (MSE), mean absolute error (MAE), and root-mean-squared error (RMSE) were compared according to the input signal intensity data obtained following the administration of the MR contrast media. As a way to provide basic data on how to administer these contrast media directly to patients, deep learning (based on machine learning) processing used the data mining software Orange (Orange3-3.34.0, University of Ljubljana, Ljubljana, Slovenia).

The software Orange is an open-source, cross-platform, machine learning toolbox used for data mining, and machine learning (http://orange.biolab.si). It features visual programming as an intuitive means of combining data analyses [25-27]. For the dataset applied to the Orange software, T1 and T2 pulse sequences were used, and signal intensities of various types of contrast media were measured and used subsequently in conjunction with deep learning to predict accurately contrast media. The signal intensities of all contrast agents were analyzed according

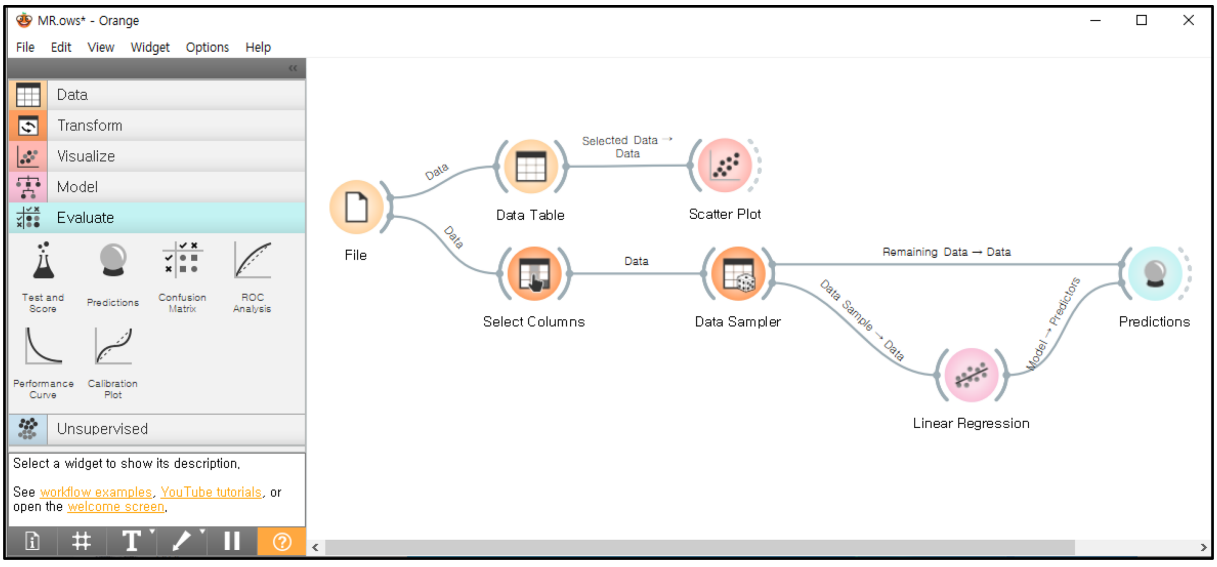


Fig. 4. (Color online) Data visualization and modeling of orange data mining software of data science toolbox. Orange software provides data analysis components and widgets, assembled into a data analysis workflow based on visual programming.

to the file, data table, and scatter plot in the software Orange, as shown in Fig. 4, and errors were analyzed in widget predictions of select columns, data sampler, linear regression, and file evaluation.

3.5. Statistical analysis

To compare the mean and 95 % confidence intervals of SNR and CNR values according to oral and ionic contrast media, ANOVA was performed with SPSS PC+ (version 20, IBM Corp., Armonk, NU, USA) and statistically significant differences were analyzed for contrast media using posthoc analyses; equal variances were not assumed. Therefore, the Dunnett T3 posthoc analysis test was used. Findings were considered to be statistically significant when the p-value was less than 0.05.

4. Results

The signal strengths of the acquired images were quantified using the image viewer; Fig. 5 shows a T1-weighted image and Fig. 6 shows a T2-weighted image. The scatter plot obtained using the software Orange for signal strength showed that canola oil had the highest value in the T1-weighted image, as shown in Fig. 7a. Additionally, the T2-weighted image in Fig. 7b indicates that blueberry juice yielded the highest value followed by apple juice.

The T1-weighted image in Table 5 yielded the highest

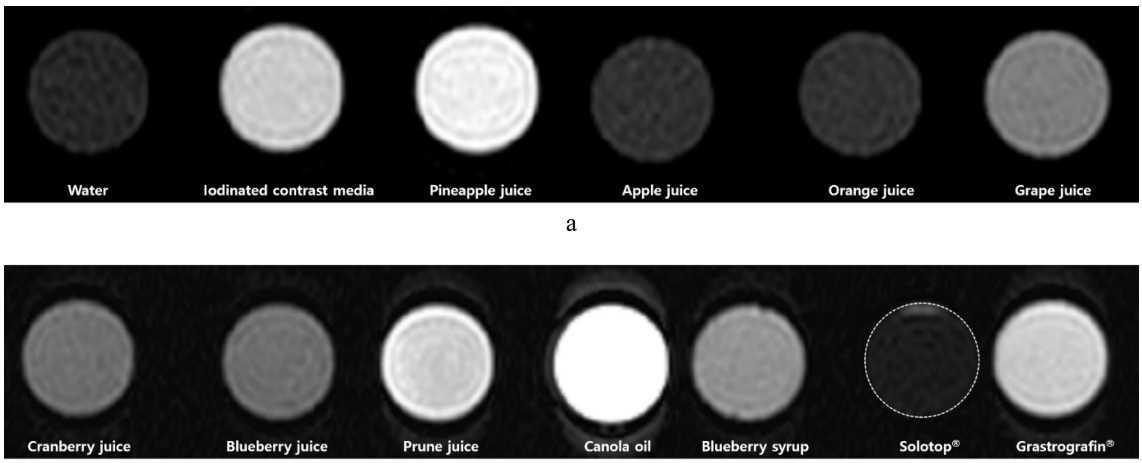


Fig. 5. T1-weighted images with contrast media of (a) (left to right) water, iodinated contrast media, pineapple juice, apple juice, orange juice, and grape juice, and (b) (left to right) cranberry juice, blueberry juice, prune juice, canola oil (highest signal intensity), blueberry syrup, Solotop® (circular dotted line), and Grastrografin®.

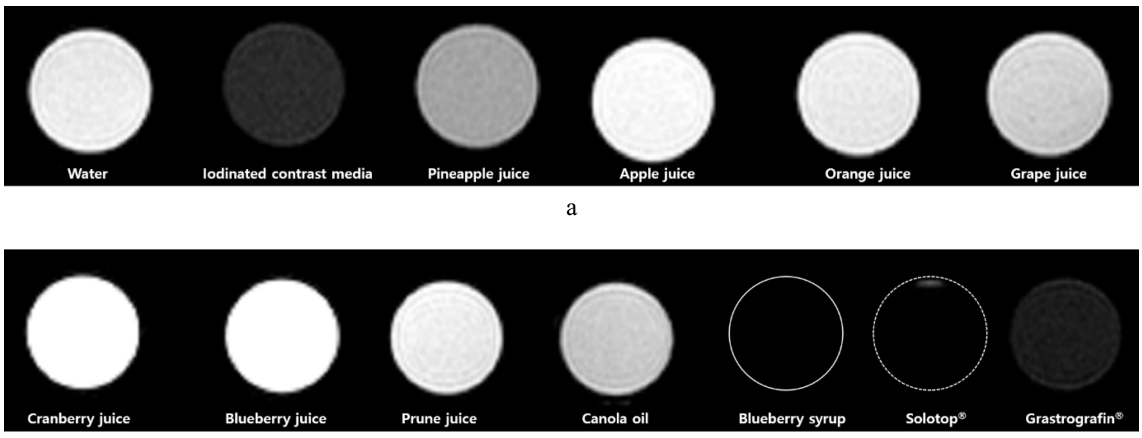


Fig. 6. Transverse relaxation (T2)-weighted images with contrast media of (a) (left to right) water, iodinated contrast media, pineapple juice, apple juice, orange juice, and grape juice, and (b) (left to right) cranberry juice, blueberry juice (highest signal intensity), prune juice, canola oil, blueberry syrup (circular line), Solotop® (circular dotted line), and Grastrografin®.

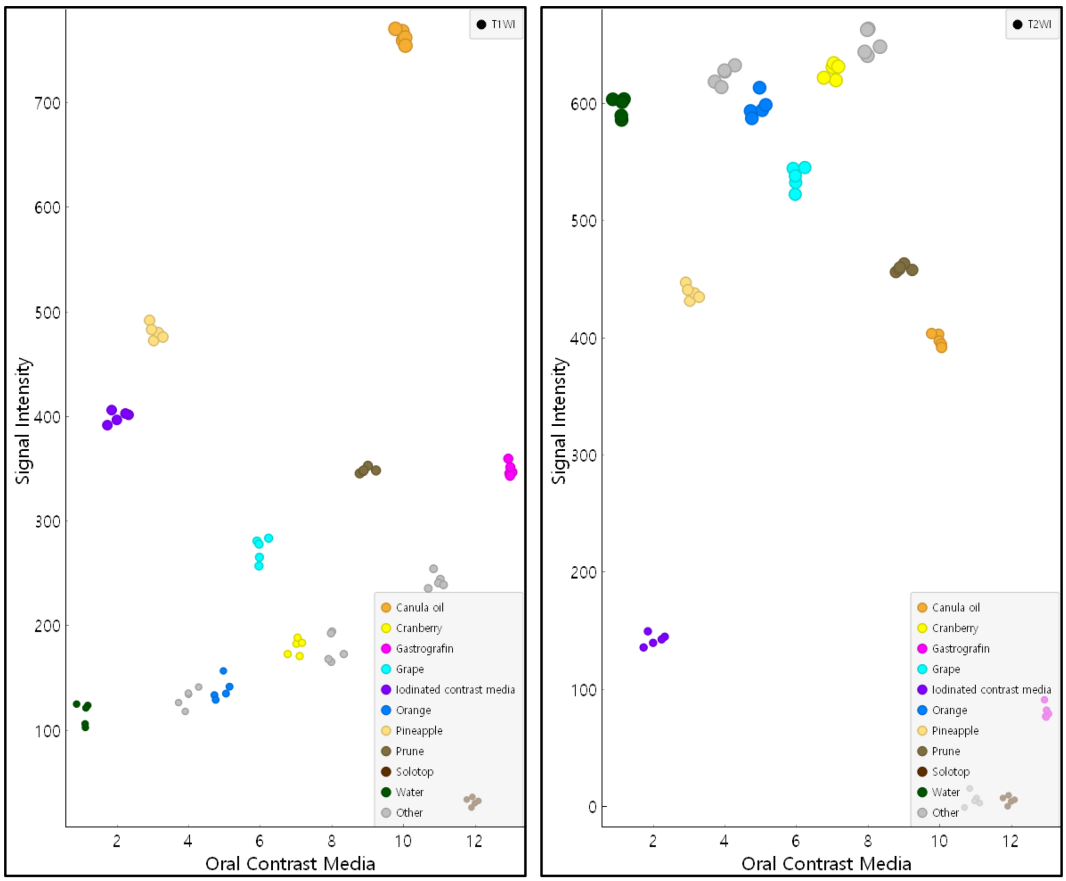


Fig. 7. (Color online) Scatter plots of image signal intensities for the contrast media based on (a) T1-weighted images of canola oil (yielded the highest signal intensity) and (b) T2-weighted images of blueberry juice (yielded a high-signal intensity).

Table 5. SNR and CNR values of T1-weighted images for various oral and chemical contrast media in the magnetic resonance pulse sequence.

Contrast Media	Signal intensity (Mean ± standard deviation (SD))	SNR	CNR	*P*-value
Water	116.24 ± 8.32	27.29		
Iodinated contrast media	404.61 ± 8.43	94.98	-67.69	
Pineapple juice	471.73 ± 9.62	110.73	-83.45	
Apple juice	133.97 ± 8.48	31.45	-4.16	
Orange juice (100 %)	136.05 ± 6.98	31.94	-4.65	
Grape juice	268.34 ± 6.72	62.99	-35.70	
Cranberry juice	182.3 ± 6.79	42.79	-15.51	<0.05
Blueberry juice (10 %)	179.06 ± 7.2	42.03	-14.75	
Prune juice	352.26 ± 12.37	82.69	-55.40	
Canola oil	763.52 ± 13.4	179.23	-151.94	
Blueberry syrup	248.85 ± 7.33	58.41	-31.13	
Solotop®	33.82 ± 5.22	7.94	19.35	
Gastrografin®	346.61 ± 7.21	81.36	-54.08	
Background	4.73 ± 4.26			

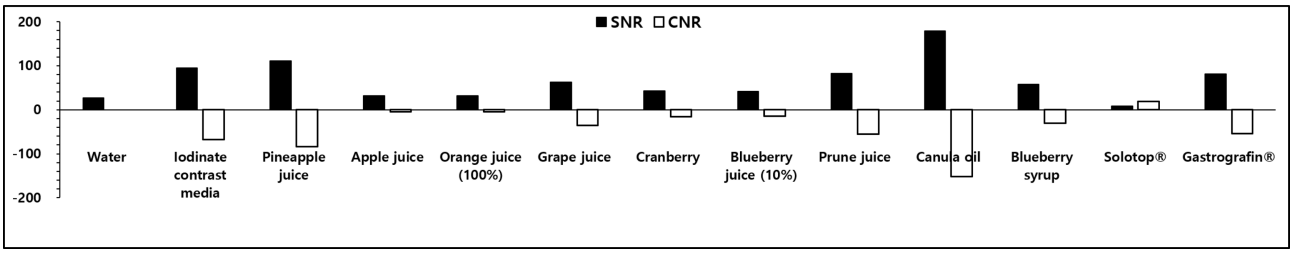


Fig. 8. Chart shows the relative signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) values of the T1-weighted images of contrast media.

SNR values (179.23 for canola oil followed by pineapple juice (110.73), iodinated contrast media (94.98), prune juice (82.69), Gastrografin® (81.36), grape juice (62.99), blueberry syrup (58.41), cranberry juice (42.79), blueberry juice (42.03), orange juice (31.94), apple juice (31.45), water (27.29), and Solotop® (7.94); measured in this order). In terms of SNR, canola oil yielded the highest SNR value, and Solotop® with water and barium sulfate yielded the lowest SNR values. CNR comparisons of contrast media were based on water. The following results were obtained: canola oil (-151.94), pineapple juice (-83.45), iodinated contrast media (-67.69), prune juice (-55.40), Gastrografin® (-54.08), grape juice (-35.70), blueberry syrup (-31.13), Solotop® (19.35), cranberry juice (-15.51), blueberry juice (-14.75), orange juice (-4.65), and apple juice (-4.16). Regarding the CNR values of T1-weighted images, the more negative the value is, the higher the contrast is. Canola oil yielded the highest CNR, and apple juice and orange juice yielded the lowest CNR. There was a statistically significant difference between water and all contrast media ($p < .05$). As shown in Fig. 8, canola oil yielded the highest SNR and CNR in T1-weighted images, and orange juice (-4.65) and apple juice (-4.16) yielded lower SNR and CNR than the other contrast media.

In the T2-weighted images (Table 6), blueberry juice had the highest SNR value of 164.29 followed by cranberry juice (158.75), apple juice (157.9), water (150.49), orange juice (149.85), grape juice (134.18), and prune juice (116.53), pineapple juice (108.48), canola oil (100.39), iodinated contrast media (36.97), Gastrografin® (19.82), blueberry syrup (2.14), and Solotop® (1.82) (measured in this order). In terms of SNR, blueberry juice yielded the highest value, whereas blueberry syrup and Solotop® yielded the lowest SNR values. Fruit-type contrast media yielded a higher SNR than those of the chemical contrast media and syrup. CNR comparisons of contrast media were based on water. The findings were: Solotop® (148.67),

Table 6. SNR and CNR values of transverse relaxation (T2)-weighted images for oral and chemical contrast media in the magnetic resonance pulse sequence.

Contrast Media	Signal Intensity (Mean ± SD)	SNR	CNR	*P*-value
Water	597.44 ± 9.13	150.49		
Iodinated contrast media	146.79 ± 7.72	36.97	113.51	
Pineapple juice	430.67 ± 7.78	108.48	42.01	
Apple juice	626.87 ± 9.12	157.90	-7.41	
Orange juice (100 %)	594.89 ± 9.73	149.85	0.64	
Grape juice	532.71 ± 13.61	134.18	16.30	
Cranberry juice	630.25 ± 9.28	158.75	-8.26	< 0.05
Blueberry juice (10 %)	652.24 ± 10.47	164.29	-13.80	
Prune juice	462.63 ± 9.2	116.53	33.96	
Canola oil	398.56 ± 8.82	100.39	50.10	
Blueberry syrup	8.51 ± 4.51	2.14	148.35	
Solotop®	7.21 ± 3.55	1.82	148.67	
Gastrografin®	78.7 ± 5.49	19.82	130.66	
Background	5.87 ± 3.97			

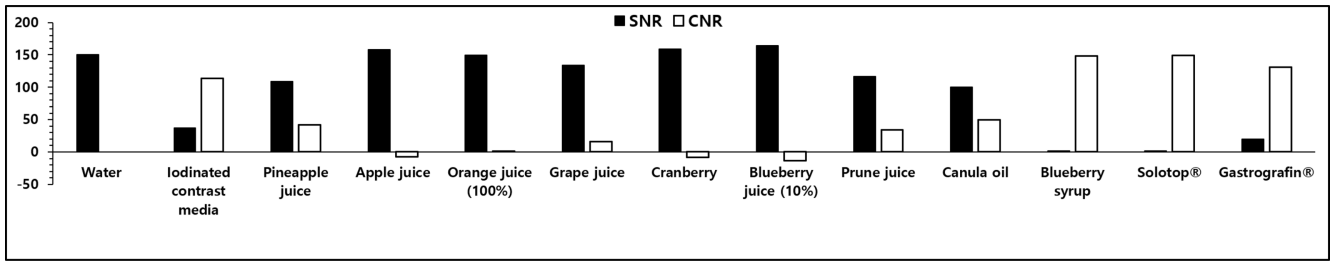
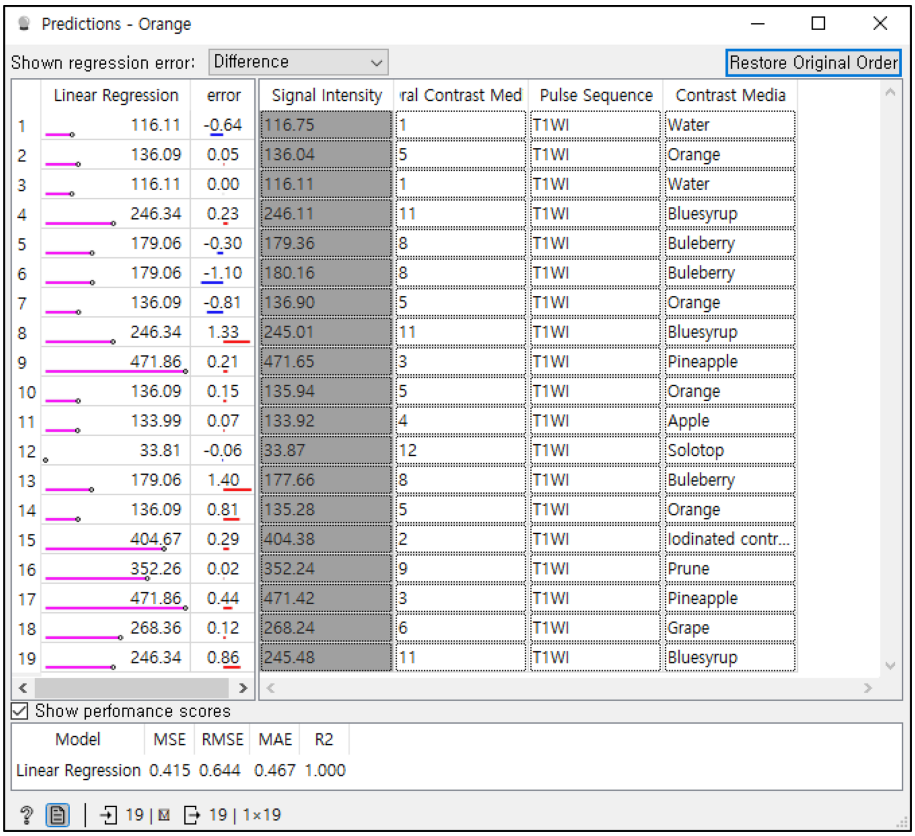


Fig. 9. Chart shows the relative SNR and CNR values of T2-weighted images of the contrast media.

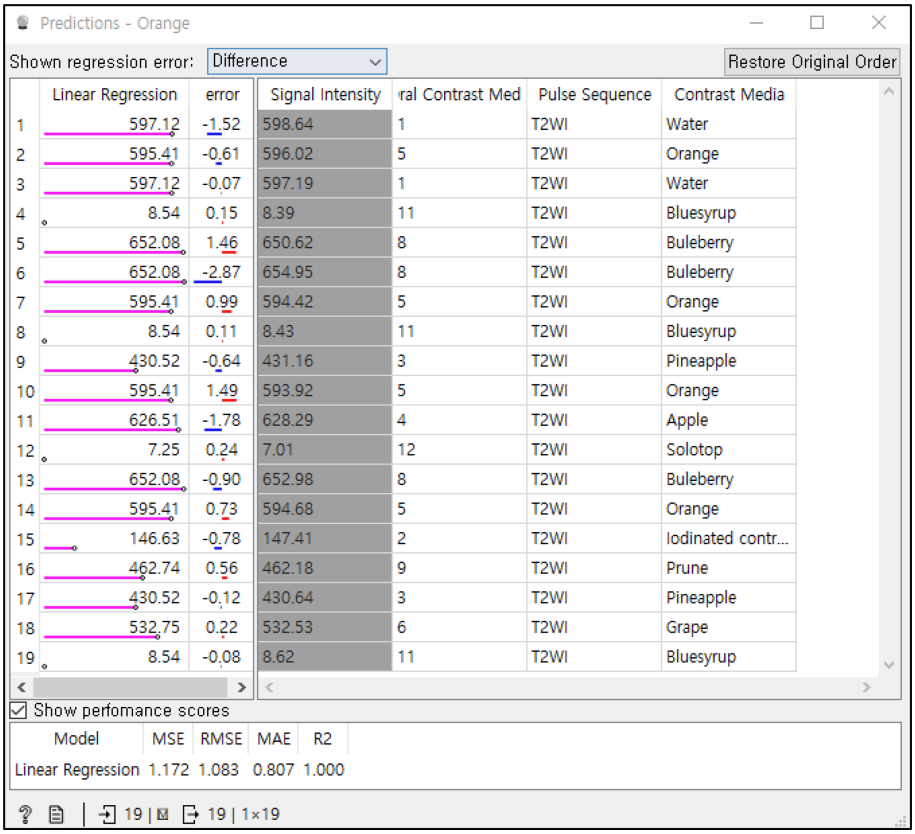
blueberry syrup (148.35), iodinated contrast media (113.51), Gastrografin® (130.66), canola oil (50.1), pineapple juice (42.01), prune juice (33.96), grape juice (16.3), blueberry juice (-13.80), cranberry juice (-8.26), apple juice (-7.41), and orange juice (0.64). Regarding the CNR values of T2-weighted images, the more negative the value is, the higher is the contrast. Solotop® (148.67) and blueberry syrup (148.35) yielded the highest values, and orange juice (0.64) yielded the lowest CNR. There was a statistically significant difference between water and all contrast media ($p < .05$). As shown in Fig. 9, blueberry juice yielded the highest SNR in the T1-weighted image and Solotop® (148.67) yielded the highest CNR.

Regarding the prediction error of deep learning for the MR signal intensities of T1-weighted images of the studied contrast media, the following results were obtained: MSE = 0.415, RMSE = 0.644, MAE = 0.467, and R^2 = 1.0, as shown in Fig. 10. In addition, in the T2-weighted image (Fig. 11), the MSE = 1.172, RMSE = 1.083, MAE = 0.807, and R^2 = 1.0, thus indicating an increased prediction accuracy.



	Linear Regression	error	Signal Intensity	ral Contrast Med	Pulse Sequence	Contrast Media
1	116.11	-0.64	116.75	1	T1WI	Water
2	136.09	0.05	136.04	5	T1WI	Orange
3	116.11	0.00	116.11	1	T1WI	Water
4	246.34	0.23	246.11	11	T1WI	Bluesyrup
5	179.06	-0.30	179.36	8	T1WI	Buleberry
6	179.06	-1.10	180.16	8	T1WI	Buleberry
7	136.09	-0.81	136.90	5	T1WI	Orange
8	246.34	1.33	245.01	11	T1WI	Bluesyrup
9	471.86	0.21	471.65	3	T1WI	Pineapple
10	136.09	0.15	135.94	5	T1WI	Orange
11	133.99	0.07	133.92	4	T1WI	Apple
12	33.81	-0.06	33.87	12	T1WI	Solotop
13	179.06	1.40	177.66	8	T1WI	Buleberry
14	136.09	0.81	135.28	5	T1WI	Orange
15	404.67	0.29	404.38	2	T1WI	Iodinated contr...
16	352.26	0.02	352.24	9	T1WI	Prune
17	471.86	0.44	471.42	3	T1WI	Pineapple
18	268.36	0.12	268.24	6	T1WI	Grape
19	246.34	0.86	245.48	11	T1WI	Bluesyrup

Fig. 10. (Color online) Predictions error of deep learning data of MSE, RMSE, MAE and R^2 for the T1-weighted MR signal image of the different contrast media.



	Linear Regression	error	Signal Intensity	ral Contrast Med	Pulse Sequence	Contrast Media
1	597.12	-1.52	598.64	1	T2WI	Water
2	595.41	-0.61	596.02	5	T2WI	Orange
3	597.12	-0.07	597.19	1	T2WI	Water
4	8.54	0.15	8.39	11	T2WI	Bluesyrup
5	652.08	1.46	650.62	8	T2WI	Buleberry
6	652.08	-2.87	654.95	8	T2WI	Buleberry
7	595.41	0.99	594.42	5	T2WI	Orange
8	8.54	0.11	8.43	11	T2WI	Bluesyrup
9	430.52	-0.64	431.16	3	T2WI	Pineapple
10	595.41	1.49	593.92	5	T2WI	Orange
11	626.51	-1.78	628.29	4	T2WI	Apple
12	7.25	0.24	7.01	12	T2WI	Solotop
13	652.08	-0.90	652.98	8	T2WI	Buleberry
14	595.41	0.73	594.68	5	T2WI	Orange
15	146.63	-0.78	147.41	2	T2WI	Iodinated contr...
16	462.74	0.56	462.18	9	T2WI	Prune
17	430.52	-0.12	430.64	3	T2WI	Pineapple
18	532.75	0.22	532.53	6	T2WI	Grape
19	8.54	-0.08	8.62	11	T2WI	Bluesyrup

Model	MSE	RMSE	MAE	R2
Linear Regression	1.172	1.083	0.807	1.000

Fig. 11. (Color online) Predictions error of deep learning data of MSE, RMSE, MAE and R^2 for the T2-weighted MR signal image of the different contrast media.

5. Discussion

MRI does not use ionizing radiation and provides quantitative data and anatomical and physiological characteristics of specific organs. However, it requires contrast media in some clinical exams. Oral contrast media are required for the visualization of the digestive tract, but these do not access the gastrointestinal tract [28]. Abdominal MRI scans produced high-quality images. In addition, when performing an abdominal MRI examination, if a contrast media is orally administered, the signal values of target tissues and blood vessels can be adjusted (by choosing the imaging parameters appropriately), thus making it easier to observe lesions.

In abdominal examinations, MRCP serves as a non-invasive, accurate, and rapid alternative [29]. The major limitations of MRCP are respiratory artifacts and poor spatial resolution; however, short acquisition times, thinner sections, and modern, high-speed imaging sequences with breath-gating and breath-holding have ameliorated the limitations. In a recent study, a patient took an oral foaming agent after MRCP (Top Effervescent-G Granules, Taejoon Pharmarceutical Co., Seoul, Korea) and water (less than 10 mL) [30]. In this study, blueberry juice yielded the highest signal strength on T2-weighted imaging followed by apple juice.

Commercially available oral contrast media for MR examinations are expensive, tasteless, and have adverse effects; blueberry and pineapple juices are now used clinically [31]. Blueberry juice in its natural pure form is not available in many countries; in patient studies it has been reported to be effective as an oral contrast media in abdominal MR in T1-weighted images [32, 33].

In this study, commercial blueberry juice was evaluated, and its signal intensity was equal to 179.06 on T1-weighted images and 652.24 on T2-weighted images; however, it did not result in statistically significant T2 signal suppression.

Pineapple juice is an alternative contrast media, but commercially available packs contain a variety of diluted juices with various levels of manganese and similar paramagnetic properties. The concentration of manganese in blueberry juice makes it effective as an oral contrast media for imaging as it suppresses gastrointestinal signals.

The relaxation-enhancing effect of blueberry juice is mainly due to Mn^{+2} ions and can be controlled by changing the Mn concentration. Manganese is one of the very few indispensable elements, and the dietary requirement for humans is in the range of 3-10 mg/day, but the amount of manganese ingested fluctuates depending on the contents of foods consumed in manganese [33]. Only 3-4% of Mn taken orally is activated and absorbed. Blueberry juice at an appropriate concentration has been reported as a contrast media that can be effectively applied to the stomach and hepatobiliary systems. In this study, fruit juice containing manganese had a lower signal intensity than canola oil on T1-weighted images and blueberry juice on T2-weighted images. Fruit juice yielded a high SNR (164.29), which is consistent with previously published results [34].

MRCP or T2-weighted images with short or intermediate TE values affect the extent of clearance of gastrointestinal fluid. The negative contrast effect of pineapple juice is due to the reduced signal intensity from gastrointestinal fluids on T2-weighted images due to the shortening of the T2 relaxation time. This appears to be a paramagnetic effect of the relatively high concentration of Mn in pineapple juice [35]. Pineapple juice is a manganese-containing negative-contrast media. Owing to its paramagnetic properties, pineapple juice is an oral contrast media that suppresses gastric juice signals and prevents overlapping artifacts in MR, thus making it an ideal alternative to chemical contrast media commonly used in MRCP testing. The use of pineapple juice as a negative contrast media has been reported to have no side effects and excellent imaging in human subjects [36, 37]. Furthermore, in Table 7, the specific values of heavy metals in oral (fruit juice) contrast media were reported based on the United States Department of Agriculture National Nutrient Database [37].

According to a study that used water, milk, and pineapple juice as oral contrast media [38], pineapple juice had excellent image quality in abdominal MR examinations, and no side effects were reported. Additional research is needed to quantify the signal strength using phantoms before its use in clinical practice. In addition, in this study, the signal intensity of pineapple juice was lower than that of canola oil on T1-weighted images, and yielded a lower signal intensity on T2-weighted images than that of sweet fruit juice [35]. In additional studies, it is necessary to use various contrast media, including pineapple juice, in clinical practice for abdominal examinations.

If an oral contrast media that is cheaper than chemical contrast media is researched and a product applicable to the human body is developed, it is expected that patients with abdominal gastrointestinal diseases can be diagnosed by MRI. Based on this experimental study, oral contrast media that are harmless to the human body were evaluated; these evaluations generated data that can be used for future oral contrast media evaluations in clinical abdominal MRI examinations.

Blueberry juice yielded the highest SNR after water in the T2-weighted images. This is because the change in signal intensity due to blueberry juice is mainly caused by Mn^{2+} ions. High Mn content has been reported for blueberry juice [37, 38]. In this experiment, the SNR and CNR values were measured using orange and blueberry juice. The SNRs of orange and blueberry juice were higher in the T2- than in the T1-weighted images, and the CNRs were similar to that of water.

The signal strength of orange juice and blueberry juice was high in the T2-weighted image because the juice itself contained an appropriate amount of water. As shown in Table 7, the oral contrast media for fruits manufactured as commercial products contained metals [39]. In addition, it was reported that date syrup containing iron in MRCP improves the visualization of images of the digestive tract as a DM-negative contrast media [40].

In MR examinations of the abdomen and MRCP, the administration of oral negative contrast media can improve the quality of examinations without increasing costs, and fruit juices, such as blueberry and pineapple, are safe to drink to improve the quality of images [41]. Based on the basic data of the results of this study, fruit juice has a higher diagnostic value than chemical contrast media in

Table 7. Contents of the different oral contrast media tested as provided by manufacturer [37].

Materials	Manufacturer	Description as purchased	Energy (kcal)	Protein (g)	Fat (g)	Iron (mg)	Manganese (mg)	Copper (mg)
Orange	Sainsbury's	Pure orange juice	47	0.5	Trace	0.12	0.04	0.02
Blueberry	Sainsbury's	Blueberry juice drink	44	0.1	Trace	0.28	0.33	0.06
Pineapple juice	Marks and Spencer	Pine juice (99 %)	35	0.5	0.1	0.29	0.92	0.11
Apple	Marks and Spencer	Pressed apple	40	0.3	0.1	0.12	0.07	0.01
Prune	Tesco	Pure prune juice	75	0.7	0.1	1.18	0.15	0.07

abdominal MR examinations and can be safely administered.

The prediction errors of deep learning for MR signal intensities in T1- and T2-weighted images using various oral contrast media yielded a MSE equal to 0.415, RMSE equal to 0.644, and a MAE equal to 0.467; all these are close to zero, thus demonstrating a highly accurate predictive function. R^2 was equal to 1.0; there was no prediction error in the signal strength accuracy. In the T2-weighted MR image, the MSE was 1.172, RMSE was 1.083, MAE was 0.807 (all are close to zero), and R2 was 1.0, thus demonstrating an increased prediction accuracy.

This study has an associated with several limitations of experimental phantom MR examination. The experimental phantom used in this study obviously cannot completely represent the human abdominal body, and unexpected effects may have influenced MRI image quality [42, 43]. Administering an oral contrast media with unknown positive signal properties, to a patient with unknown signal properties of digestive system content provides a wide range of variables [39]. However, Zarrini *et al.* [44] reported that natural oral contrast media (pineapple juice, blueberry juice, etc.) can be effectively applied to the digestive system by reporting advantages over artificial contrast media, including taste and tolerability. First, MR scans were performed using commercially available fruit juices, water, and contrast media; however, additional evaluations are needed based on comparisons with oral and chemical contrast media used in clinical practice. Second, no comparisons were conducted with various oral and chemical contrast media that are used in MR abdominal examinations, and there are no comparisons of signal strength, SNR, and CNR using various MR pulse sequences. Third, commercial fruit juices were used, but additional analyses and evaluations using various components are needed.

In spite of these limitations, the prediction function with high accuracy was shown in the prediction error of deep learning for the MR signal intensity of various contrast agents in the T1-weighted image and the T2-weighted image, and the prediction error in the signal intensity showed accuracy. Therefore, this preliminary phantom study can serve as a basis for abdominal MR and MRCP examination, and it is expected that continuous discussions will be made and used as a reference for the development of new oral contrast media.

6. Conclusion

Depending on the MR contrast media, signal intensity, SNR, and CNR were measured differently in T1- and T2-weighted images. In T1-weighted images, the signal strength and SNR were highest in canola oil followed by pineapple juice (which contained manganese), and CNR was measured in canola oil and pineapple juice. In the T2-weighted images, blueberry and apple juice yielded high SNR values, and CNR was high for Solotop® and blueberry syrup. Fruit juice yielded a relatively high-contrast effect compared with water and chemical contrast media. In MR examinations of the abdomen, the contrast media are substances with different signal intensities in different sequences, and the signal intensities differ depending on the administered substance. In the T1- and T2-weighted images, high-accuracy predictions were demonstrated in terms of the prediction error of deep learning pertaining to the MR signal intensities of various contrast media.

In conclusion, for abdominal MR examinations, an appropriate contrast media should be selected according to the availability of the contrast media and clinical conditions (including the patient's status). Based on the MRI examinations conducted in this study, it is expected that generated data from ex vivo studies will continue to be used for the development of new oral contrast media.

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