Deep-Learning-Based Feature Encoding of Clinical Parameters for Patient Specific CTA Dose Optimization

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Abstract. The use of contrast agents in CT angiography examinations holds a potential health risk for the patient. Despite this, often unintentionally an excessive contrast agent dose is administered. Our goal is to provide a support system for the medical practitioner that advises to adjust an individually adapted dose. We propose a comparison between different means of feature encoding techniques to gain a higher accuracy when recommending the dose adjustment. We apply advanced deep learning approaches and standard methods like principle component analysis to encode high dimensional parameter vectors in a low dimensional feature space. Our experiments showed that features encoded by a regression neural network provided the best results. Especially with a focus on the 90% precision for the "excessive dose" class meaning that if our system classified a case as "excessive dose" the ground truth is most likely accordingly. With that in mind a recommendation for a lower dose could be administered without the risk of insufficient contrast and therefore a repetition of the CT angiography examination. In conclusion we showed that Deep-Learning-based feature encoding on clinical parameters is advantageous for our aim to prevent excessive contrast agent doses.

Keywords: Feature encoding · Deep Learning · Case-based reasoning · Contrast agent

1 Introduction

Feature encoding is a preprocessing step used in many machine learning applications to reduce the dimension of the input feature vectors. The process of feature encoding removes redundant data so more meaningful or relevant features can be derived from the raw inputs. This can yield a higher accuracy of the given task.

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A well-known feature encoding technique is the principle component analysis (PCA) which represents the data as a linear combination of features with the greatest variance. In [14] the PCA is used to encode high dimensional genome expressions to predict the clinical outcome of breast cancer. Advancing to non-linear encoding techniques Deep Learning methods came in to focus. In [11] the authors implemented an autoencoder to encode surface meshes of segmented hippocampi to subsequently classify whether the patient suffers from Alzheimer's disease. This area of non-linear feature encoding also includes the variational autoencoder. The authors of [12] used this approach to extract features for the detection of pathologies while the authors of [10] trained a variational autoencoder to reduce the dimension of single tumor cells for differentiating between tumor subpopulations.

In this paper we propose a comparison between different means of feature encoding applied to clinical parameters for a classification task (Fig. 1). In this way a recommendation to reduce the standard dose can be made which is a part of the primary objective to adjust the dose of contrast agent (CA) used in CT angiographies (CTA) for each patient individually. This is based on the fact that CAs often contain in iodine that can cause harmful side effects including anaphylactic reactions and thyrotoxicosis [1,2]. It poses a risk especially to the renal system with contrast-induced renal nephropathy being the third leading cause of hospital acquired acute renal failure [9]. Unnecessarily high CA doses should therefore be avoided in order to minimize the health risk of the patient as well as saving expenses for CA. However, often a standard dose is administered in clinical practice. A previous method uses the body weight and a weight factor to compute an individualized CA dose [5]. Another approach tested a weight-based protocol incorporated with the tube potential selection to lower the CA dose [13].

In contrast, we considered a greater set of clinical parameters in addition to the body weight with the goal to give the medical practitioner an improved dose adjustment recommendation with respect to a standard dose. We compared different methods of Deep-Learning-based feature encoding including amongst others a variational autoencoder (VAE) and a regression neural network (RNN). As an already established feature encoding method we implemented a principal component analysis (PCA) to compare with the advanced techniques. For the evaluation of the influence of the encoded features on the dose prediction quality we used a k-Nearest-Neighbour (kNN) classification on the raw input features. Each method is used as a preprocessing step for kNN-based classification in one of two classes: 1) Non-excessive image contrast, 2) Excessive image contrast.

The determination of the classes and therefore the image contrast were previously executed. Based on Regions of Interest (ROI) set in CTA volumes a rule-based assessment was implemented. This assessment acts as the ground truth for the feature encoding classification.

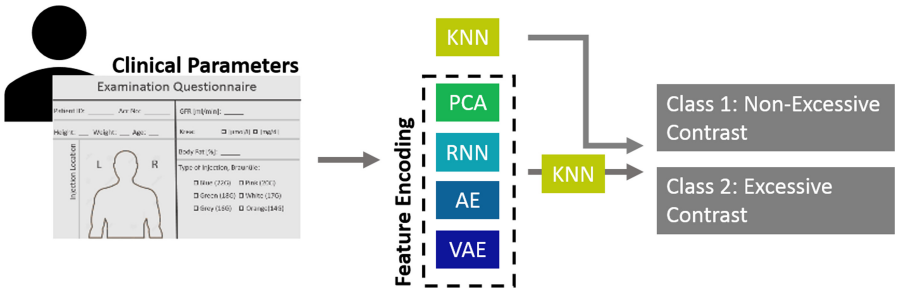

Fig. 1. Clinical parameters were encoded using the following methods: principle component analysis (PCA), regression neural network (RNN), autoencoder (AE) and variational autoencoder (VAE). The classification was implemented with k-Nearest-Neighbour (kNN). As a base comparison the kNN was used on the raw features.

2 Data

The clinical parameters and the corresponding CTA volumes were sourced from the radiology department of the UKSH Lübeck. All 76 CTA examinations were limited to the aorta area. The patients received a CA dose of 100 mL of the CA Imeron 300. Additionally, 20 clinical parameters were collected including body weight, height and blood pressure at rest among others.

To build the ground truth for the classification through feature encoding a quality assessment of the image contrast was executed. An overview of the assessment is displayed in Fig. 2. Experts placed three ROIs at predefined locations in axial CTA slices. The ROIs were defined to lie equally spaced across the CTA volume in order to encompass the entire contrast-enhanced area. Taking the mean HU values of each ROIs rules were applied resulting in the two aforementioned contrast classes.

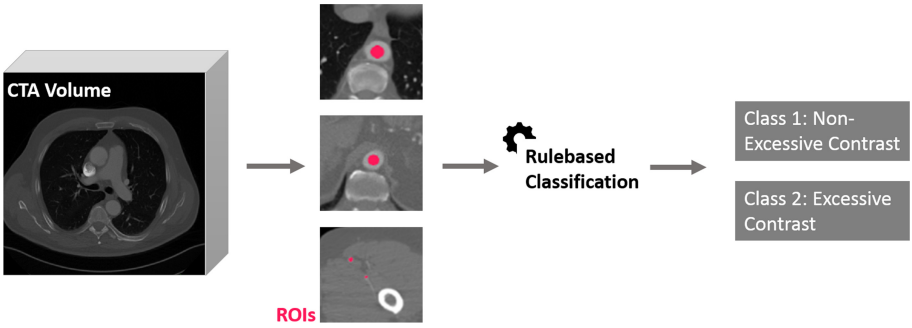

Fig. 2. ROIs are placed in axial slices of a CTA volume. Through a rule-based classification the image contrast class is determined.

3 Methods

3.1 Autoencoders

Autoencoders (AEs) [7] are neural networks, that consist of two parts: an encoder $Q(X)$, which maps the input X to a latent vector $\mathbf{z} \in \mathrm{R}^m$ and a decoder $P(\mathbf{z})$ that tries to reconstruct the input X given only $\mathbf{z}$. To ensure $X \approx P(Q(X))$ a reconstruction loss is applied, e.g. L1-loss. The latent space mapping makes autoencoders suitable for feature encoding, since the latent representation $\mathbf{z}$ is assumed to contain all the important information about the input. The feature encoding can be established by directly inputting an unseen vector in the trained encoder and considering its latent encoding.

3.2 Variational Autoencoders

Variational autoencoders (VAEs) [7] are an extension of conventional autoencoders assuming a prior distribution of the latent space. Typically a normal distribution $\mathbf{z} \sim \mathcal{N}(0, 1)$ is enforced by using an additional loss function D_{KL} (Kullback-Leibler Divergence), which measures the distance between the predicted latent space distribution and the chosen a-priori distribution. To assure a normal distribution, the encoder predicts a mean μ and a standard deviation σ and the latent vector is calculated $\mathbf{z} = \mu + \epsilon\sigma$, where $\epsilon \sim \mathcal{N}(0, 1)$.

3.3 Regression Neural Network

Regression or classification neural networks are frequently used as feature extractors by considering the outputs of intermediate layers [8]. While AEs and principle component analysis generate rather general features describing the most important properties of an input, the intermediate outputs of networks solving particular tasks rather concentrate on features that are problem-specific. In order to generate features that describe the probability of a particular set of clinical parameters to fit in a certain class, in this work, we consider regression to the mean values of the three ROIs (Fig. 2) [6]. The last hidden layer is then used as feature extractor.

3.4 Implementation Details

The neural networks are implemented using PyTorch in a fully-connected manner. The autoencoders contain three encoding and two decoding layers and map the input vectors of length 20 to a latent vector of length 5. In our experiments this length turned out to be optimal, while choosing lengths between 12 (number of modes in PCA) and 5 delivered worse results. The regression neural network features 4 fully-connected layers, whereas the last hidden layer maps the input to a feature length of 5 in a similar manner. An important detail is the augmentation of the inputs and regressed values by adding noise sampled from a

normal distribution with standard deviation 0.3. Also, the input parameter vectors were standardized for all experiments. For linear feature encoding principle component analysis is also applied as reference method and to compare it with Deep-Learning-based feature encoding methods (Fig. 3).

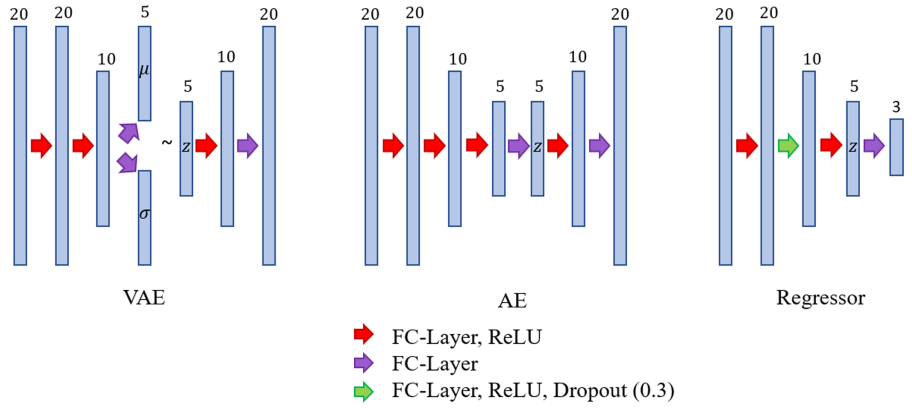

Fig. 3. Architectures of the neural networks. From left to right: VAE, AE, regression network. z denotes the feature encoding layer. For details see the legend on the bottom.

3.5 PCA

In this work, inspired by statistical shape models (SSMs) [3], principal component analysis (PCA) is used for dimensionality reduction and feature encoding of the clinical parameters. PCA is typically applied on discrete shape representations $X_1 \dots X_n$ of a training dataset, where each representation consists of landmark positions. However, here every X_i is represented by a vector of clinical parameters. The main steps for the feature encoding are the following: 1) Compute the mean vector over all shapes $X_\mu = 1/n \sum_{i=1}^{n} X_i$. 2) Apply PCA: Build a covariance matrix $\mathbf{C} = 1/n \sum_{i=1}^{n} (X_i - X_\mu)(X_i - X_\mu)^T$ and compute its eigenvectors u_p and corresponding eigenvalues λ_p: $Xu_p = \lambda_p u_p$. Since the eigenvectors corresponding to the largest eigenvalues describe the main variation in the data, only the first m eigenvectors are used in the following and the rest is omitted. Here, m is chosen to cover 95% of the variability of the training dataset resulting in 12 modes. New forms can now be described using this model as follows $X_{new} = X_\mu + \mathbf{U}c$, where $\mathbf{U} = [u_1 \dots u_m]$, $c = [c_1 \dots c_m]^T$ and c_j are coefficients for each eigenvector that can be varied. However, to reconstruct an unseen form X' using $X' = X_\mu + \mathbf{U}c'$, a coefficient vector $c' = \mathbf{U}^T(X' - X_\mu)$ needs to be found. Since those coefficients describe the input vector in an unambiguous dimensionality-reduced manner, they can be used as feature encodings of the clinical parameters.

3.6 KNN Contrast Classification

For the classification of the individual contrast class for CA dose adjustment recommendations the kNN classification was used. The k-Nearest-Neighbour method [4] is an intuitive way to classify previously unseen data. kNN is considered as an instance-based learning algorithm as its learning consist of storing the training data in the feature space. The algorithm assumes that samples of the same classes lie in close proximity of each other. To classify an unseen sample a distance to all stored data is computed. Different distance measures are applicable for example the Euclidean distance. The class of the new instance is determined as the most frequent class among the k nearest data. k should be neither too low or too high as the algorithm becomes susceptible to outliers or neglects classes with a small number of data points respectively. In this work, kNN is used for the classification of the following computed features and also directly on the input data. In our experience, for the feature encoding scenario kNN with $k = 5$ and an Euclidean distance delivered best classification results, however for using the kNN on the raw features $k = 3$ with a correlation distance measure was chosen.

4 Results

The results for the classification are shown in Table 1. All experiments are conducted in a leave-one-out manner and the values are averaged over the different training sets. For evaluation different values are calculated, that take into account the number of true positive (TP), false positive (FP), false negative (FN) and true negative (TN) classifications per class (excessive vs. non-excessive contrast agent).

$$Precision = \frac{TP}{TP + FP}$$

$$Recall = \frac{TP}{TP + FN}$$

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN}$$

$$F1\text{-}Score = 2\frac{Precision \times Recall}{Precision + Recall}$$

Note that the accuracy measure is the only one considering true negative values (patients are correctly classified as not class-related). For this reason the values for the accuracy might be high even if the precision and recall are considerably poor, e.g. PCA, AE and VAE feature encoding (Table 1). The best feature-encoding results are achieved with the regression method, since this method is more task-related, compared to the autoencoding methods. Interestingly, when using the regression-based features for classification better accuracy and F1-score are achieved compared to applying the rule-based classification to the regressed values. This is due to the fact, that features contain more abstract information and are less affected by noise or other small artifacts and errors.

Overall, the regression-based feature encoding delivers high accuracy and recall with an accent especially on the precision for class 2 (excessive contrast). With a precision of 0.9 the system is in a large proportion of cases capable to rightfully assign class 2, meaning that a recommendation to lower the CA dose can be given without risking a repeated scan due to insufficient image contrast.

Table 1. Comparison of classification results using different feature encoding techniques. From top to bottom: **raw data** - kNN directly on the raw input data vectors; **PCA** - kNN on PCA-extracted features; **Reg-Features** - kNN on features extracted with a regression network; **Reg-Class** - classification of HU values predicted by a regression network; **AE** -kNN on features extracted from the z-space of an autoencoder; **VAE** - kNN on features extracted from the z-space if a variational autoencoder. The measurements are calculated per class (class 1: non-excessive contrast; class 2: excessive contrast).

Method	Accuracy		Precision		Recall		F1-score	
	Class 1	Class 2	Class 1	Class 2	Class 1	Class 2	Class 1	Class 2
Raw data	0.78	0.78	**1**	0.77	0.15	**1**	0.26	0.86
PCA	0.73	0.73	0	0.73	0	**1**	0	0.84
Reg-Features	**0.89**	**0.89**	0.87	**0.90**	**0.72**	0.96	**0.79**	**0.93**
Reg-Class	0.88	0.88	0.92	0.87	0.61	0.98	0.73	0.92
AE	0.73	0.73	0.5	0.75	0.17	0.94	0.30	0.82
VAE	0.70	0.70	0	0.72	0	0.96	0	0.84

5 Discussion and Conclusion

In this work, we aim to establish a case-based reasoning for CTA contrast agent dose based on sets of clinical parameters. We presented different machine learning methods for feature encoding from clinical parameters. Encoded features are used in a kNN-based classification for determining whether a recommendation for using less contrast agent than the standard dose should be made. The feature encoding methods feature (variational) autoencoders a regression neural network and a PCA compared to directly classifying the raw data. Since the regression-based feature encoding is task-based, it delivers the best accuracy (0.89). Autoencoding and PCA-based methods deliver more general features, that cannot be classified with such high accuracy. Even though the used approaches are rather naive, a reliable recommendation can be made based on the regression method. However, the methods of this work will be adapted and improved in future work to enhance the result even more. We will consider a variety of architectural decisions and also a more sophisticated classification method as well as experiments with subsequent feature selection techniques. Future work will also include the exact dose determination based on this first recommendation to adapt the CA dose.

References

1. Andreucci, M., Solomon, R., Tasanarong, A.: Side effects of radiographic contrast media: pathogenesis, risk factors, and prevention. BioMed Res. Int. **2014**, 20 p. (2014). Article number: 741018
2. Becker, C.: Radiologisch praxisrelevante Prophylaxe und Therapie von Nebenwirkungen jodhaltiger Kontrastmittel. Der Radiologe **47**(9) (2007). Article number: 768. https://doi.org/10.1007/s00117-007-1550-4
3. Cootes, T.F., Taylor, C.J., Cooper, D.H., Graham, J.: Active shape models-their training and application. Comput. Vis. Image Underst. **61**(1), 38–59 (1995). https://doi.org/10.1006/cviu.1995.1004
4. Cover, T., Hart, P.: Nearest neighbor pattern classification. IEEE Trans. Inf. Theory **13**(1), 21–27 (1967)
5. Feng, S.T., et al.: An individually optimized protocol of contrast medium injection in enhanced CT scan for liver imaging. Contrast Media Mol. Imaging **2017**, 8 p. (2017). Article number: 7350429
6. Hannan, S.A., Manza, R.R., Ramteke, R.J.: Generalized regression neural network and radial basis function for heart disease diagnosis. Int. J. Comput. Appl. **7**(13), 7–13 (2010). https://doi.org/10.5120/1325-1799
7. Kingma, D., Welling, M.: Auto-encoding variational Bayes, December 2014
8. Lai, Z., Deng, H.: Medical image classification based on deep features extracted by deep model and statistic feature fusion with multilayer perceptron. Comput. Intell. Neurosci. **2018** (2018). https://doi.org/10.1155/2018/2061516
9. Pannu, N., Wiebe, N., Tonelli, M., Network, A.K.D., et al.: Prophylaxis strategies for contrast-induced nephropathy. JAMA **295**(23), 2765–2779 (2006)
10. Rashid, S., Shah, S., Bar-Joseph, Z., Pandya, R.: Dhaka: variational autoencoder for unmasking tumor heterogeneity from single cell genomic data. Bioinformatics (2019)
11. Shakeri, M., Lombaert, H., Tripathi, S., Kadoury, S.: Deep spectral-based shape features for Alzheimer's disease classification. In: Reuter, M., Wachinger, C., Lombaert, H. (eds.) SeSAMI 2016. LNCS, vol. 10126, pp. 15–24. Springer, Cham (2016). https://doi.org/10.1007/978-3-319-51237-2_2
12. Uzunova, H., Schultz, S., Handels, H., Ehrhardt, J.: Unsupervised pathology detection in medical images using conditional variational autoencoders. Int. J. Comput. Assist. Radiol. Surg. **14**(3), 451–461 (2018). https://doi.org/10.1007/s11548-018-1898-0
13. Vasconcelos, R., et al.: Reducing iodine contrast volume in CT angiography of the abdominal aorta using integrated tube potential selection and weight-based method without compromising image quality. Am. J. Roentgenol. **208**(3), 552–563 (2017)
14. Zhang, D., Zou, L., Zhou, X., He, F.: Integrating feature selection and feature extraction methods with deep learning to predict clinical outcome of breast cancer. IEEE Access **6**, 28936–28944 (2018)