Effect of Bayesian penalty likelihood algorithm on 18F-FDG PET/CT image of lymphoma

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\textbf{Objective}  Recently, a new Bayesian penalty likelihood (BPL) reconstruction algorithm has been applied in PET, which is expected to provide better image resolution than the widely used ordered subset expectation maximization (OSEM). The purpose of this study is to compare the differences between these two algorithms in terms of image quality and effects on clinical diagnostics and quantification of lymphoma.

\textbf{Methods}  A total of 246 FDG-positive lesions in 70 patients with lymphoma were retrospectively analyzed by using BPL and OSEM + time-of-flight + point spread function algorithms. Visual analysis was used to evaluate the effects of different reconstruction algorithms on clinical image quality and diagnostic certainty. Quantitative analysis was used to compare the differences between pathology and lesion size.

\textbf{Results}  There were significant differences in lesion-related SUV\textsubscript{max}, total-lesion-glycolysis (TLG), and signal-to-background ratio (SBR) ($P < 0.01$). The variation $\Delta$ SUV\textsubscript{max}\% and $\Delta$ SBR\% caused by the two reconstruction algorithms were negatively correlated with tumor diameter, while $\Delta$ MTV\% and $\Delta$ TLG\% were positively correlated with tumor diameter. In the grouped analysis based on pathology, there were significant differences in lesion SUV\textsubscript{max}, lesion SUV\textsubscript{mean}, and SBR. In non-Hodgkin’s lymphoma (diffuse large B cells and follicular lymphoma), diversities were significantly found in SUV\textsubscript{max}, SUV\textsubscript{mean}, SBR, and TLG of the lesions ($P < 0.05$). According to the grouped analysis based on lesion size, for lesions smaller than 1 cm and 2 cm, there was a significant difference in SUV\textsubscript{mean}, SUV\textsubscript{max}, SBR, and MTV, but not in lesions larger than or equal to 2 cm ($P > 0.05$), and the liver background SUV\textsubscript{mean} ($P > 0.05$) remained unchanged.

\textbf{Conclusion}  BPL reconstruction algorithm could effectively improve clinical image quality and diagnostic certainty. In quantitative analysis, there were no significant differences among different pathological groups, but there were significant diversities in lesion sizes. Especially for small lesions, lesion SUV\textsubscript{max} increased and SBR was significantly improved, which may better assist in the diagnosis of small lesions of lymphoma. \textit{Nucl Med Commun} 43: 284–291 Copyright © 2021 The Author(s). Published by Wolters Kluwer Health, Inc.

\textbf{Keywords:} Bayesian penalty likelihood, FDG, lymphoma, PET, SUV

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\textbf{Received} 5 August 2021 \textbf{Accepted} 16 November 2021

\textbf{Introduction}  Background: PET and 18F-deoxyglucose (18F-FDG) are widely used in oncology diagnosis, staging, disease recurrence, and patient management. Lymphoma, in particular, clinically relies on PET/computed tomography (CT) to quantify the overall disease burden and evaluate treatment response, as well as treatment guidance [1]. At the end of the relevant course of treatment, PET/CT can be used to evaluate the effectiveness of treatment and to determine whether there are residual signs of the tumor [2]. Especially for small lesions, the detection rate was limited by partial volume effect (PVE) and traditional reconstruction techniques that cannot achieve complete convergence, which may cause a lower signal-to-noise ratio and poor visual detectability. In the past decade, PET technology has made some progress, including new hardware functions, such as time-of-flight (TOF) acquisition [3] and advanced image reconstruction methods of point spread function (PSF) [4], so that PET images have been substantially improved. The detectability of lesions and standardized uptake value (SUV) of lymph nodes of ordered subset expectation maximization (OSEM) reconstruction with TOF and PSF were better than those of conventional OSEM reconstruction [5]. In recent years, GE Healthcare (Milwaukee, USA) proposed a new iterative image reconstruction algorithm called Q.Clear [6], which combines the Bayesian penalty likelihood (BPL) algorithm. Q.Clear considers all aspects of the image reconstruction process, including PSF modeling and an innovative penalty factor [7], so that the algorithm can achieve complete convergence [8]. The penalty function

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is controlled by a penalty factor called $\beta$, which is the only variable in the algorithm that can be modified by the operator. Therefore, compared with OSEM reconstruction, the SUV value obtained by the BPL algorithm is more accurate than that obtained by OSEM, and the image resolution is higher, which has great potential in enhancing 18F-FDG PET image quality [9]. The purpose of this study is to compare the traditional OSEM + TOF + PSF reconstruction algorithm with the latest BPL algorithm and to investigate their effects on the image quality, clinical diagnosis, and quantitative analysis of lymphoma.

Materials and methods

Clinical data

The data of consecutive cases examined by 18F-FDG PET/CT in the PET/CT center of our hospital from March 2020 to December 2020 were retrospectively analyzed. There were 42 males and 28 females. The average age was $51.67 \pm 16.09$-years old (range 19–83 years), and the average BMI was $24.58 \pm 4.03$ (range: 14.88–33.91). There were eight cases of Hodgkin's lymphoma and 62 cases of non-Hodgkin’s lymphoma, including 31 cases of diffuse large B cells, 18 cases of follicular lymphoma, and 13 cases of other types.

18F-FDG PET/CT image acquisition and analysis

The subjects were under normal fasting conditions for more than 6 hours and their blood glucose was less than or equal to $11.1$ mmol/L. 18F-FDG was injected with a dose of $3.67 \pm 0.01$ g MBq/kg. The acquisition began 60 mins after injection using Discovery 710Clarity PET/CT (GE Healthcare, Milwaukee, USA). Body PET scans were performed from the base of the skull to the upper part of the femur. PET collection parameters were 1.5 min/bed, free-breathing, matrix $192 \times 192$. CT collection parameters were layer thickness, $3.75$ mm, voltage $120$ kVp, auto mA:30–180. PET reconstruction used OSEM (three iteration/24 subsets, 6.4 mm Gaussian filter) + TOF + Sharp IR (PSF), and BPL mode ($\beta = 570$). BPL is Q.Clear by GE Healthcare, Milwaukee, USA and $\beta$ is the regularization factor, of which the function is to regulate the regularization effect [11]. The data obtained were divided into two groups of different reconstruction algorithms (OSEM + TOF + PSF and BPL), and the differences in metabolic parameters were compared. Using pathology as the distinctive criteria, data were then divided into four subgroups: Hodgkin, diffuse large cell B, follicular, and others. Finally, data were divided into three groups of different lesion sizes: long-axis diameter less than 1 cm, 1–2 cm, or more than 2 cm. The reconstructed PET/CT images were processed by the AW4.7 workstation (GE Healthcare, Milwaukee, USA). The long-axis diameter (D) of the lesion on the fused image was measured. Lesions were delineated according to the 42% threshold method, and the normal background tissue was selected using spherical volumes-of-interest (VOIs), with a diameter of 1 cm in the right posterior lobe of the liver, while avoiding the location of tumor focus, inflammation, hyperplasia, and other lesions. The metabolic parameters of VOIs, including focus SUVmean, SUVmax, metabolic tumor volume (MTV), and calculate total-lesion-glycolysis (TLG), liver SUVmean-liver and tissue signal-to-back ratio [signal-to-background ratio (SBR)] to evaluate the image quality of PET/CT were recorded. The difference rate of SUVmax, SBR, MTV, and TLG in BPL and non-BPL groups were calculated at the same time, such as $\Delta\text{SBR%} = \frac{\text{SBR}_{\text{BPL}} - \text{SBR}_{\text{non-BPL}}}{\text{SBR}_{\text{non-BPL}}} \times 100\%$.

Two experienced nuclear medicine doctors (with 10 and 15 years of experience in nuclear medicine, respectively) were asked to evaluate the image quality of the 70 positive lymphoma lesions on PET images reconstructed randomly and sequentially by OSEM and BPL methods, using a 4-point scale:

1. Poor, the lesions were not visible, and the degree of 18F-FDG uptake was below the background.
2. Moderate, the degree of 18F-FDG uptake is higher than that of background, but it is difficult to distinguish from noise.
3. Good, the uptake of 18F-FDG is higher than that of the background and can be distinguished from noise.
4. Excellent, good significance, higher 18F-FDG uptake than the background, can be distinguished from noise, and the perimeter of focus can be defined.

At the same time, a 4-point rating scale was also used to evaluate the certainty of image quality for diagnosis:

1. Poor, uncertainty, image was not helpful for diagnosis.
2. Moderate, lesions were shown, but the diagnostic accuracy was not strong.
3. Good, good certainty, lesions were clearly shown and helped for the clinical diagnosis.
4. Excellent, high certainty of diagnosis.

The evaluation of the two observers was conducted independently, did not know the clinical information and PET reconstruction methods, and was distinguished only by clinical experience.

Statistical analysis

All the data are expressed following the mean $\pm$ SD, and statistical analysis is carried out by using the SPSS22.0 software (IBMCo., New York, USA). The image quality and diagnostic score were compared by nonparametric rank-sum test. The metabolic parameters of different reconstruction techniques, pathological subgroups, and lesion size groups were compared by the $t$-test and one-way ANOVA. The relationship between the change rate of metabolic parameters and diameter produced by the two reconstruction methods was analyzed by Pearson
correlation analysis. The difference was statistically significant when $P < 0.05$.

**Results**

The characteristics of all patients and reconstructed data are shown in Table 1. In this study, 70 patients included 246 FDG-positive lesions, with an average size of $1.56 \pm 0.31$ cm.

**Visual analysis results**

The consistency intraclass correlation coefficient of the two observers was 0.706 ($P < 0.001$). The distribution of image quality and diagnostic certainty was shown in Fig. 1. About 17.61% and 21.83% of the lesions can not be visualized or provide effective clinical diagnostic information on the images of non-BPL reconstruction algorithms, while the lesions using the BPL reconstruction algorithm accounted for 94.37% and 63.38%, respectively. These differences were statistically significant ($P < 0.001$) (Fig. 2).

**The results of quantitative analysis between different reconstruction techniques groups**

The statistical results of metabolic parameters between the two groups according to different reconstruction parameters are shown in Table 2. There was no significant difference in background SUVmean uptake and lesion metabolic volume MTV between the two groups using the BPL algorithm and OSEM + TOF + PSF algorithm, but there was a significant difference in lesion-related SUVmax, TLG, and SBR between the two groups ($P < 0.05$). The results of correlation analysis between the change of metabolic parameters and lesion diameter were shown in Table 3. $\Delta$ SUVmax% and $\Delta$ SBR% were negatively correlated with tumor diameter, while $\Delta$ MTV% and $\Delta$ TLG% were positively correlated with tumor diameter.

**Comparison of metabolic parameters among different pathological groups**

The data distribution and paired t-test comparison results were shown in Table 4 and Fig. 3. In the first group of Hodgkin lymphoma, there was no significant difference in liver background SUVmean, MTV, TLG, but diversities were found in lesion SUVmax, SUVmean, and SBR between the two reconstruction algorithms. In the second group and the third group of lesions with non-Hodgkin’s lymphoma (the pathological types were diffuse large B and follicular type, respectively), there was no significant difference in liver background SUVmean, MTV between the two reconstruction algorithms, but diversities were found in lesion SUVmax, SUVmean, SBR, and TLG. In the fourth group (other pathology), significant differences were found in lesion SUVmax and liver background SUVmean. There was no significant difference in $\Delta$ SUVmax%, $\Delta$ SBR%, $\Delta$ MTV%, $\Delta$ TLG% among different pathological groups.

**Comparison of metabolic parameters with different lesion sizes**

For lesions smaller than 2 cm, there was a significant difference in SUVmean, SUVmax, SBR, and MTV between BPL and OSEM + TOF + PSF reconstruction algorithms, but there was no significant difference in SUVmean, SUVmax, SBR, and MTV in lesions larger than or equal to 2 cm ($P > 0.05$). However, there was no significant difference in liver background SUVmean among the three groups ($P > 0.05$). TLG was only affected by the reconstruction algorithm in the lesions smaller than 1 cm ($P < 0.05$) and larger than 2 cm ($P < 0.01$) (Table 5).

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**Table 1 Basic information of the examinee**

| Clinical info | Clinical data |
|---------------|--------------|
| Gender female/male (%) | 28 (40%)/42 (60%) |
| Age (years-old) | 51.67 ± 16.09 (19–83) |
| BMI (kg/m²) | 24.58 ± 4.03 (14.88–33.91) |
| The dose of 18F-FDG (MBq/kg) | 3.67 ± 0.01 (3.65–3.69) |
| Glucose (mmol/l) | 5.88 ± 1.03 (4.7–11) |
| Diagnostic (Pathology) | | |
| Hodgkin (%) | 8 (11.43%) |
| Non-Hodgkin (%) | 62 (88.57%) |
| Diffuse large B cells (%) | 31 (44.29%) |
| Follicular lymphoma (%) | 18 (25.71%) |
| others(%) | 13 (18.57%) |

**Fig. 1**

Visual scores of clinical image quality and diagnostic certainty using Bayesian penalty likelihood (BPL) and non-BPL algorithms.

**Table 2**

| Clinical info | Clinical data |
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**Fig. 2**

Visual scores of clinical image quality and diagnostic certainty using Bayesian penalty likelihood (BPL) and non-BPL algorithms.
Discussion

In the past few years, many reconstruction algorithms have been introduced to reduce errors and artifacts, which affect the quality of clinical images, as well as the accuracy and repeatability of quantitative parameters SUV. At present, the clinical standard for PET image reconstruction is an iterative algorithm, mainly an OSEM algorithm, which has a tradeoff between the number of subsets and image quality: each subset contains less tomography and statistical information, so noise and artifacts will increase [10]. To achieve the complete convergence of the image in the process of reconstruction, multiple iterations are needed; however, with the increase of the number of iterations, the background noise will also increase. On the contrary, because the reconstruction of the image is limited to reducing noise, it can not achieve complete convergence, thus reducing the accuracy and quality of the PET image. With the development of technology, the technology of TOF and PSF is gradually improved, and the spatial resolution is partially compensated. TOF mainly improves the SNR through temporal resolution [11] but does not affect the standardized uptake value (SUV) [5], while PSF mainly improves the spatial resolution of reconstruction [12]. In clinical studies, SUVmax increases by more than 30% [13]. Both TOF and PSF are beneficial to the tradeoff between (CR) and SNR, but all these reconstruction methods (OSEM + TOF + PSF) have a limitation in principle, that is, to obtain sufficient contrast recovery by increasing the number of iterations/subsets will be at the cost of reducing SNR.
The BPL reconstruction algorithm considers all aspects of the image reconstruction process, including PSF modeling and an innovative penalty factor. The penalty factor is a function, which is given by the value difference between adjacent voxels and the sum of them. As a noise suppression, the algorithm achieves complete convergence and provides a high SNR for the image. In each iteration, compared with voxels with higher noise, voxels with smaller changes between adjacent voxels are slightly advantageous. BPL can regulate the image through the penalty factor \( \beta \), and the selection of \( \beta \) can affect the comparison results between different algorithms. Reynés-Llompart et al. conducted a model test using GE Discovery IQ PET/CT [14]. Under the NEMA NU-2012 standard, it was found that compared with PSF or OSEM (both without TOF), the CNR of the image reconstruction process, including PSF or OSEM (both without TOF), the CNR of the image through the penalty factor \( \beta \) was improved.

Table 2: Statistical results of metabolic parameters between two groups with different reconstruction parameters

| Quantitative parameter | BPL | Non-BPL | P-value |
|------------------------|-----|---------|---------|
| Lesion SUVmax          | 15.25 ± 10.17 | 12.97 ± 7.87 | 0.000 |
| Lesion MTV             | 4.18 ± 7.10  | 4.29 ± 6.37  | 0.273 |
| Lesion TLG             | 43.00 ± 104.58 | 39.36 ± 93.41 | 0.000 |
| Background liver SUVmean | 2.52 ± 0.27  | 2.51 ± 0.30  | 0.558 |
| SBR                    | 6.02 ± 4.13  | 5.14 ± 3.54  | 0.000 |

BPL, Bayesian penalty likelihood; MTV, metabolic tumor volume; SBR, signal-to-background ratio; SUV, standardized uptake value; TLG, total-lesion-glycolysis.

Table 3: Correlation analysis between the change of metabolic parameters and the diameter of lesions

| ΔSUVmax% (16.92% ± 29.12%) | ΔSBR% (19.30% ± 30.92%) | ΔMTV% (30.31% ± 85.55%) | ΔTLG% (6.60±6% ± 68.80%) |
|-----------------------------|--------------------------|------------------------|--------------------------|
| −0.187                     | −0.177                   | 0.13                   | 0.13                     |
| 0.003                      | 0.05                     | 0.04                   | 0.04                     |

ΔSUVmax%, ΔSBR%, ΔMTV%, ΔTLG% = % change between adjacent values. P-value = probability value.

MTV, metabolic tumor volume; SBR, signal-to-background ratio; SUV, standardized uptake value; TLG, total-lesion-glycolysis.

Table 4: Results of metabolic parameters among different pathological groups

| Nodules (number) | 1 = Hodgkin | 2 = Diffuse large B | 3 = Follicular | 4 = Others |
|------------------|-------------|---------------------|--------------|-----------|
| Nodules (number) | 59          | 103                 | 69           | 16        |
| SUVmax-BPL       | 15.8 ± 1.20 | 1.72 ± 1.59         | 1.46 ± 0.51  | 0.91 ± 0.35 |
| ΔSUVmax%         | −0.187      | −0.177              | −0.138       | 0.13       |
| ΔSBR%            | −0.177      | 0.005               | 0.04         | 0.04       |
| ΔMTV%            | 0.13        | 0.04                | 0.04         | 0.04       |
| ΔTLG%            | −7.59%      | −37.83%             | −13.63%      | −22.28%    |

BPL, Bayesian penalty likelihood; MTV, metabolic tumor volume; SBR, signal-to-background ratio; SUV, standardized uptake value; TLG, total-lesion-glycolysis.
Fig. 3

Diagram of metabolic parameters among different pathological groups.

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It has been confirmed that the new algorithm BPL had little effect on the liver background. Although the background noise in the liver was higher under PSF reconstruction [20] than BPL, generally TOF and PSF had little effect on the liver and mediastinal uptake [21]. In a clinical study of colorectal cancer liver metastasis [22], the BPL reconstruction algorithm improved the SNR and SBR of colorectal cancer liver metastasis detected by 18F-FDG-PET/CT and increased the lesion SUVmax without changing the background SUV or image noise of the liver. In the clinical application of lymphoma, PET/CT is often used in mid-treatment and post-chemotherapy evaluation, using the Deauville score (DeauvilleScore, DC) to distinguish between responders and nonresponders [23]. DC is a visual assessment criterion to classify the malignant/benign nature and to quantify the treatment response. The strongest uptake of lymphoma lesions was compared with the physiological uptake of mediastinal blood pool and liver (background) to evaluate the response to treatment. DS1–3 is defined as responder and DS4–5 is defined as nonresponders [1]. Because of the improvement of SBR, the BPL algorithm is more effective in the detection of medium and low background (such as mediastinal lymph nodes and pulmonary nodules). However, because it affects the value of SUVmax in small lesions [24], but does not significantly affect the background value, it may overestimate the overall tumor load, thus changing the classification of DS [25]. Enilorac et al. [26] recently studied whether the choice of reconstruction methods affected the DS. In their study of 126 patients, although different reconstruction methods led to changes in DS in a small number of patients, Kaplan–Meier analysis showed that there were statistical differences in progression-free survival and overall survival between responders and nonresponders, no matter which reconstruction method was used for intertreatment and posttreatment PET imaging. It was suggested that the risk stratification of 18F-FDG-PET in patients with diffuse large B-cell lymphoma was not affected by the selective reconstruction algorithm, because the 2-y PSF and OS were similar. In another study [27], including all types of lymphoma, not just diffuse large B-cell lymphoma, they also found significant differences in DS classification in some patients with BPL algorithm and concluded that it needed further research to determine which reconstruction algorithm is better to evaluate the prognosis of lymphoma. In our study, the pathology of all lymphomas was included. The differences in liver background and SBR in other pathological groups may be due to the small sample size and small lesions in this group. In the subtypes of lymphoma with high FDG metabolisms, such as DLBCL, HL, and FL, the BPL algorithm had a significant effect on the SUVmax, SUVmean, and SBR of the lesions. Therefore, when comparing the DS scores of different centers, we still need to consider the consistency of the reconstruction algorithm.

In the past few years, PET was used as a routine in radiotherapy planning and clinical treatment response evaluation. At present, the traditional method is to measure the MTV of lesions according to the threshold. In this experiment, a 40% threshold was selected to determine the lesion volume. It was found that different pathologies had no obvious effect on MTV, but the size of lesions was related to the measurement of MTV. For lesions whose diameters were less than 2 cm, the BPL algorithm had a greater impact on MTV. This might be related to the PVE and the Gibbs artifact caused by BPL reconstruction [16]. In the BPL algorithm, there is no post-filtering processing, only by increasing the penalty factor $\beta$ to generate a smoother image, so the relationship between MTV and $\beta$ selection needs to be further studied. Moreover, MTV measurement could be affected by the contour algorithm [28]. Although there are other voxel-based threshold methods [29], which have a good advantage only for lesions with strong heterogeneity, and for areas with low contrast, the new contour algorithm may become unstable. More research on the impact of MTV will be carried out in the future. Many previous studies have reported PET semiquantitative parameters such as SUVmax or MTV as potential prognostic imaging markers in cancer patients [30,31]. Through effective complete convergence, the BPL reconstruction algorithm can represent more accurately these parameters in the future. Although the sample size of this retrospective study was not large enough, we have shown that, especially for small lesions, SBR has been significantly improved and lesion SUVmax has increased significantly, which may better assist in the clinical diagnosis of small lesions of lymphoma.

| Table 5 Comparison of metabolic parameters of different lesion sizes |
|------------------|-----------|-----|------|-------|
| Diameter         | Parameter | Mean | SD   | T     |
| D < 1 cm         | SUVmax    | 3.31 | 5.97 | 4.33  |
|                  | SUVmean   | 1.72 | 9.00 | 0.000 |
|                  | MTV       | 0.39 | 2.73 | 4.15  |
|                  | Liver SUVmean | 0.01 | 0.21 | 0.31  |
|                  | TLG       | 0.98 | 3.68 | 2.09  |
|                  | SBR       | 1.23 | 2.42 | 3.97  |
|                  | SUVmax    | 2.27 | 4.50 | 6.05  |
|                  | SUVmean   | 1.92 | 2.43 | 14.23 |
|                  | MTV       | 0.30 | 1.09 | 3.31  |
|                  | Liver SUVmean | 0.01 | 0.17 | 0.99  |
|                  | TLG       | 0.63 | 5.89 | 1.28  |
| 1 cm < D < 2 cm  | SUVmax    | 0.92 | 3.05 | 1.96  |
|                  | SUVmean   | 0.64 | 4.95 | 5.54  |
|                  | MTV       | 0.86 | 2.95 | 1.87  |
|                  | Liver SUVmean | 0.01 | 0.17 | 0.57  |
|                  | TLG       | 20.59 | 32.56 | 4.10  |
|                  | SBR       | 0.37 | 2.25 | 1.05  |
| D > 2 cm         | SUVmax    | 3.31 | 5.97 | 4.33  |
|                  | SUVmean   | 1.72 | 9.00 | 0.000 |
|                  | MTV       | 0.39 | 2.73 | 4.15  |
|                  | Liver SUVmean | 0.01 | 0.21 | 0.31  |
|                  | TLG       | 0.98 | 3.68 | 2.09  |
|                  | SBR       | 1.23 | 2.42 | 3.97  |
|                  | SUVmax    | 2.27 | 4.50 | 6.05  |
|                  | SUVmean   | 1.92 | 2.43 | 14.23 |
|                  | MTV       | 0.30 | 1.09 | 3.31  |
|                  | Liver SUVmean | 0.01 | 0.17 | 0.99  |
|                  | TLG       | 0.63 | 5.89 | 1.28  |
|                  | SBR       | 0.87 | 2.00 | 5.24  |

MTV, metabolic tumor volume; SBR, signal-to-background ratio; SUV, standardized uptake value; TLG, total-lesion-glycolysis.
Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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