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Optimizing bladder volume to minimize OAR dose in cervical cancer HDR intracavitary brachytherapy: an experimental and analytical dosimetric investigation

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Abstract

This study aims to determine the optimal bladder volume that can balance the dose distribution to the organs-at-risk (OARs), specifically the bladder and rectum, and to analyze the relationship between variations in bladder volume and the dose received by these two organs during high-dose-rate (HDR) brachytherapy. Six bladder volume variations, namely empty, 100 cc, 150 cc, 200 cc, 250 cc, and 300 cc, were used to analyze the correlation between bladder volume and the radiation dose received by the bladder and rectum. An experimental approach was employed by observing the dose point distribution and the D2cc dose to both organs based on calculations from the Treatment Planning System (TPS), which were then compared with analytical calculations using a quadratic polynomial regression model via the Ordinary Least Squares (OLS) method. In general, the bladder point dose and D2cc dose increased with increasing bladder volume; however, the rectal dose demonstrated very high stability (90-100 cGy). Based on the variations in bladder volume, the optimal volume was 100 cc, as it protects the bladder by minimizing dose distribution and stabilizes the dose to the rectum. The statistical analysis results showed that the quadratic regression model had a high goodness-of-fit to the experimental data, with a coefficient of determination (R^2) value of 0.92.

Keywords: bladder volume; cervical cancer; organs at risk; D2cc.

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INTRODUCTION

Brachytherapy is a highly effective radiation therapy for cervical cancer treatment, as it can deliver a high local dose to the tumor with a rapid dose fall-off to the surrounding healthy tissue (Azahari et al. 2022; Geraldo et al. 2021). Furthermore, brachytherapy is considered the most suitable therapy for cancers located in complex anatomies surrounded by radiosensitive organs, such as cervical cancer, prostate cancer, and uterine cancer (Fuentealba and Santibáñez 2020). The success of brachytherapy

in cervical cancer is determined not only by the dose delivered to the target but also depends on the protection of organs-at-risk (OARs) such as the bladder, rectum, and sigmoid colon, which are located very close to the radiation source (Sadeghic et al. 2018; Safigholi et al. 2018; Zakariaee and Mahdavi 2015). Excessive exposure to OARs can lead to both acute and chronic side effects, such as radiation cystitis, rectal bleeding, or gastrointestinal dysfunction, which impact the patient's quality of life (Xu et al, 2021). Therefore, controlling the dose to OARs through critical dose parameters such as D_2cc is key in cervical brachytherapy to achieve an optimal balance between tumor control probability (TCP) effectiveness and the minimization of normal tissue complication probability (NTCP) (Haidari et al. 2019; Jacob et al. 2017).

In cervical cancer brachytherapy procedures, the bladder and rectum are the closest organs at risk to the radiation source. Variations in bladder volume can cause significant anatomical changes, including shifts in organ position and deformation of the target volume (CTV). These geometric alterations can lead to discrepancies between the planned radiation dose and the dose actually delivered to the tumor, thereby increasing dosimetric uncertainty and potentially reducing clinical accuracy and therapeutic effectiveness (Lu and Wang 2019; Mahantshetty et al. 2017; Ye, Zhao, and Sun 2023; Zakariaee and Mahdavi 2015). Fuccio *et al*., (2015) reported that radiotherapy in the pelvic area causes common side effects in at least 50% of cancer patients, with symptoms such as diarrhea, abdominal pain, rectal bleeding, and urinary urgency, where the bladder and rectum are the most vulnerable organs (Fuccio, Frazzoni, and Guido 2015).

Several studies have reported the influence of bladder filling on the dose to the target area and the doses to OARs, particularly the bladder, colon, and sigmoid (Khan 2003; Lu and Wang 2019; Sharma et al. 2018; Ye, Zhao, and Sun 2023). Sharma et al (2018) confirmed that the dose to the bladder increases with its volume, while the doses to the rectum and sigmoid colon peak at a bladder volume of 70–110 cc. The lowest doses to these organs were recorded when the bladder volume exceeded 170 cc (Sharma *et al*., 2018). Another study reported that restricting bladder volume during brachytherapy can reduce the dose to the bladder; however, this may cause the small intestine or sigmoid colon to descend into the pelvic cavity and move closer to the applicator, potentially increasing the dose to these organs (Xu et al., 2021). The mean bladder dose increased significantly with greater bladder filling, whereas all small intestine doses decreased significantly. Thus, bladder volume is a controllable factor influencing radiotherapy dose distribution (Lu and Wang 2019). However, previous research findings have relied heavily on treatment planning systems (TPS) calculations and patient image datasets, often without validation through experimental phantom measurements or comprehensive analytical models, which fail to account for tissue interactions and applicator positioning.

The need to clinically validate brachytherapy dose distribution is becoming increasingly important, given the dynamic anatomical changes that occur, such as variations in bladder volume. Dose calculations in TPS that still rely on the TG-43 approach have limitations, as they do not fully consider these changing anatomical factors, thereby potentially affecting the accuracy of clinical dose estimates (Wu et al. 2021)(Haidari et al. 2019). Here, analytical calculations provide a solution to evaluate the suitability of the dose distribution generated by TPS and measurement. Therefore, the dose distribution in clinical brachytherapy procedures needs to be validated using alternative approaches, one of which is through analytical calculations and measurement.

This validation aims to evaluate the consistency between the dose distribution model generated by the planning system and a more idealized mathematical approach. Cross-validation also ensures the accuracy of therapy planning results, thereby reducing dosimetric uncertainty and guaranteeing that the

delivered radiation dose conforms to the plan. This ensures optimal therapeutic effectiveness against the tumor target while minimizing the risk of complications to surrounding organs. Several studies have reported that analytical calculations (Bechchar, Senhou, and Ghassoun 2019; Bielajew 2000; Han et al. 2014) as well as other methods like Monte Carlo simulations (Wu et al. 2021; Zakariaee and Mahdavi 2015) erve as benchmark methods for assessing the accuracy of treatment planning systems.

Changes in dose distribution due to variations in bladder volume require a more reliable validation approach to prevent serious complications in organs at risk. In response to this, the study employed an experimental validation method using phantoms with varying bladder volumes, which were subsequently verified using analytical methods. This study evaluates the dose distribution and D2cc dose to the bladder and small intestine across different bladder volumes to support the treatment planning process for cervical cancer brachytherapy. The aim is to ensure the delivered radiation dose remains optimal for the tumor target while minimizing the risk to OARs. The uniqueness of this study lies in its experimental approach using a plastisin phantom with varied bladder fillings, validated with an analytical method. This setup allows for controlled simulation of clinical conditions. It provides dosimetric insights that can serve as a foundation for developing safer, more consistent clinical protocols through bladder volume management during brachytherapy.

METHODS

Phantom and Bladder Model

In this study, the phantom used for the experiment was a custom-made cube (20 cm × 20 cm × 20 cm) constructed from plastisin. Plastisin is a wax-based material chosen as a patient substitute medium because it has a density or Hounsfield Unit (HU) value that is close to the HU value of soft tissue in the body. Soft tissue generally has a value of around +40 HU to +80 HU, while plasticine itself has a CT value of around 55 HU. The use of a 20 cm × 20 cm × 20 cm plasticine phantom provides a controlled, uniform environment that is easy to place the applicator in. This standardized geometry was employed to minimize variations in patient anatomy and geometry. The model was equipped with a dedicated chamber for bladder filling and a channel for applicator placement, as illustrated in Figure 1. Variations in bladder volume were simulated using a balloon filled with distilled water, with six different volume conditions: empty (filled with air), 100 cc, 150 cc, 200 cc, 250 cc, and 300 cc. Variable control was implemented to ensure that the observed changes in dose distribution and the D2cc to the bladder and rectum were primarily attributable to bladder volume variations. The result was achieved by controlling for other factors influencing dose distribution, including applicator orientation, patient/phantom anatomical geometry, and the treatment planning techniques used in the TPS.

Verification of the dose point and applicator geometry is performed through virtual reconstruction on the TPS. Phantom images are used to create a virtual model for the placement of the applicator and source, allowing for precise determination of their geometry and position. After the reconstruction process, the best view configuration for the intrauterine and ovoid applicators is determined. Next, a Co-60 source simulation is performed by setting the control point, dwell position, and dwell time at each irradiation point. These settings enable the accurate modeling of source movement and dwell time, allowing for a quantitative analysis of the dose distribution.

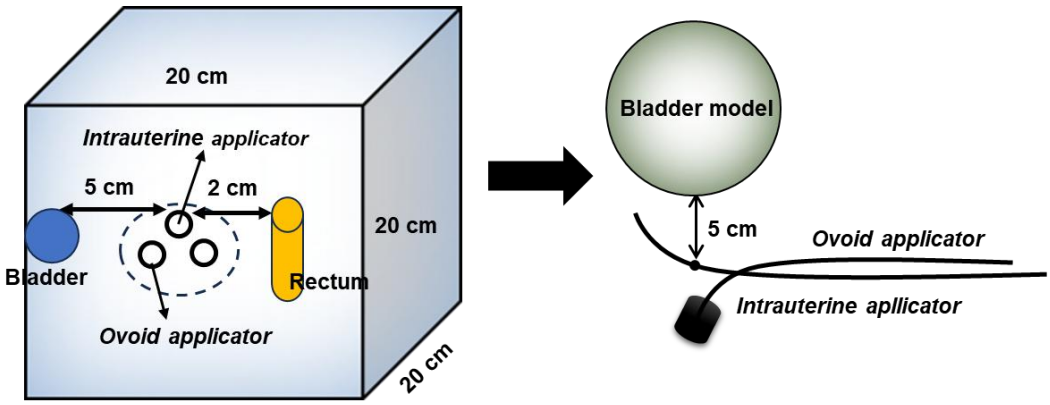

Figure 1. Phantom set up for dose measurement.

The intrauterine applicator was positioned within the phantom at a distance of 5 cm from the bladder and 2 cm from the rectum. The bladder model was then placed into a dedicated compartment designed for this purpose. Subsequently, the entire phantom configuration underwent CT scanning to evaluate the influence of bladder volume variations on geometrical and positional changes. The resulting CT images served two primary purposes: (1) to visualize geometrical changes in the bladder and its position relative to both the applicator and the rectum, and (2) to perform calculations of the dose distribution at specific points within the bladder and the D2cc dose to the organs at risk (OARs), specifically the bladder and rectum. Point dose calculations for the bladder were performed at the posterior, middle, and anterior walls. The point dose and D2cc values were determined using the SagiPlan treatment planning system with an HDR brachytherapy Co-60 radiation source.

The D2cc dose calculation for the bladder and rectum was performed based on the CT scan images of the phantom using the SagiPlan treatment planning system. The process began with delineating (contouring) the bladder and rectum on the CT images to define the anatomical boundaries of these two organs at risk (OARs). Subsequently, the intrauterine applicator was reconstructed from the CT images into a virtual model to define its position and configuration within the phantom precisely. The dose distribution was then simulated by configuring the parameters for the Co-60 radiation source, specifically by setting the control points and dwell times for each position along the applicator. Finally, based on this simulation, the absorbed D2cc dose values for the bladder and rectum were obtained directly from the software's calculation output.

Dose Determination Using an Analytical Approach

Determining the D2cc dose to the bladder integrated calculations from the SagiPlan Treatment Planning System (TPS), and with an analytical approach. The analytical approach was a corrective and cross-validation method to minimize potential deviations in the TPS results. Specifically, the functional relationship between variations in bladder volume (the independent variable) and the D2cc values (the dependent variable) was modeled using a second-order polynomial regression. The quadratic model was selected based on its ability to represent the anticipated non-linear relationship between volume and dose response, with the quadratic regression equation applied as per Equation 1.

$$\hat{Y}_i = a + bX_i + cX_i^2 \quad (1)$$

With $\widehat{Y}_i$ is the value predicted by the analytical model for the D2cc value; the coefficients a, b, and c are the intercept, linear coefficient, and quadratic coefficient, X_i is the variation of bladder volume. These coefficients were determined using the Ordinary Least Squares (OLS) method to minimize the sum of the squared differences between the dose values predicted by the model and the TPS-calculated results. This optimization process involves formulating the following system of normal equations:

$$\Sigma Y = na + b\,\Sigma X + c\,\Sigma X^2 \quad (2)$$

$$\Sigma XY = a\,\Sigma X + b\,\Sigma X^2 + c\,\Sigma X^3 \quad (3)$$

$$\Sigma X^2 Y = a\,\Sigma X^2 + b\,\Sigma X^3 + c\,\Sigma X^4 \quad (4)$$

This system of linear equations was subsequently solved in matrix form to obtain the values of coefficients a, b, and c. The resulting mathematical model not only demonstrates strong concordance with experimental data but also enables the prediction and identification of the optimal bladder volume that yields the safest dose distribution to the OARs. The evaluation of the degree of conformity between TPS dose calculations and analytical modeling was analyzed using linear regression. The accuracy of the regression model was validated by calculating the coefficient of determination (R^2) in Excel.

RESULTS AND DISCUSSION

Bladder Geometry Variation

In brachytherapy techniques, the D_2cc dose is utilized as a reference or constraint for organs at risk (OARs) because this parameter represents the maximum dose received by a 2 cm³ tissue volume. It is thus clinically recognized as being sensitive to the risk of radiation side effects in critical organs surrounding the treatment target (Dagli, Yurt, and Yegin 2020; Han et al. 2014). The D2cc dose does not represent a specific point; it is the estimated maximum dose delivered to a 2 cm³ tissue volume, making its precise anatomical location impossible to determine. Therefore, control points are required to estimate the dose delivered to specific locations within the bladder. Measurement points in the bladder are typically divided into three areas: posterior (A), middle (B), and anterior (C). The dose distribution at these bladder control points is illustrated in Figure 2.

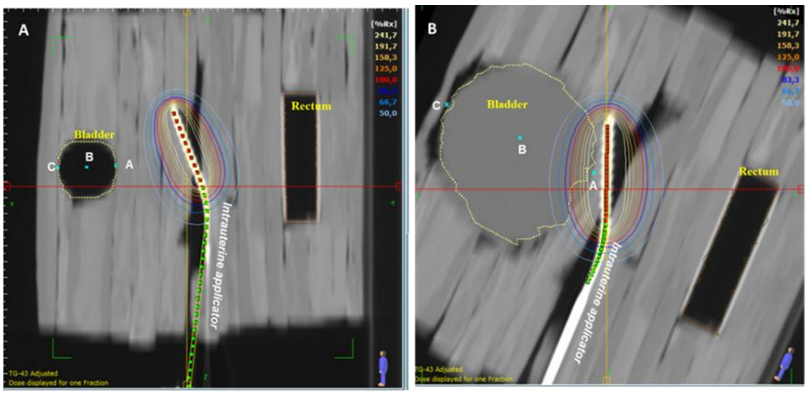

Figure 2. Variation in dose distribution of the HDR brachytherapy source for (a) an empty bladder and (b) a bladder filled with 300 cc.

Variations in bladder volume were demonstrated to have a systematic effect on the magnitude of

the absorbed dose at the bladder control points in the cervical cancer brachytherapy simulation. The simulation results indicate a general trend where an increase in bladder volume is followed by an increase in dose to the bladder itself. The phenomenon can be explained by changes in the geometry and relative position of the bladder in relation to the radiation source applicator. When the bladder is empty or contains air, the received dose is at its minimum. This occurs because the bladder positions (anterior, middle, and posterior) are farther from the radiation source. Furthermore, the presence of air, a low-density medium, reduces interaction with radiation, cumulatively resulting in lower dose absorption. This is confirmed by the analysis of CT-scan images in Figure 2. Bladder filling causes the organ to expand and shift, bringing its critical regions-especially the posterior wall, which is anatomically closest to the intrauterine applicator-closer to the radiation source. The point doses to the bladder across different bladder volumes are presented in Figure 3.

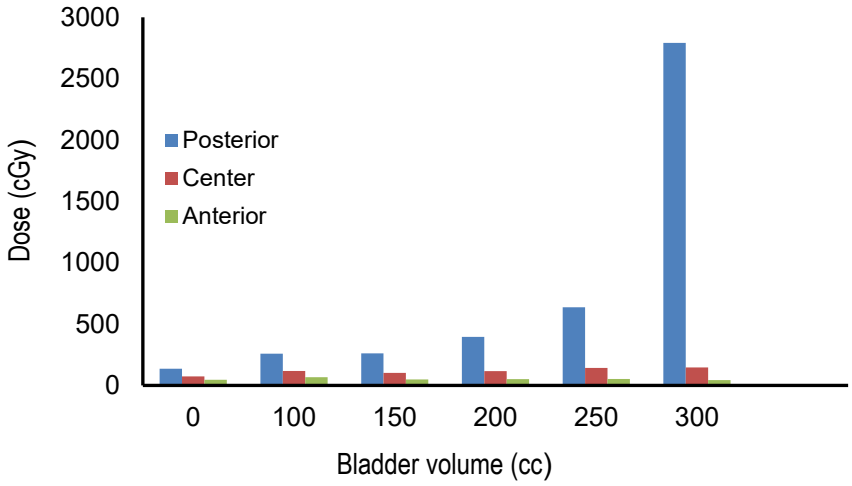

Figure 3. Dose distribution at the bladder control points (posterior, center, and anterior) at variations in bladder volume.

The point dose at the posterior bladder wall consistently received the highest dose compared to the central and anterior regions across all six bladder volume variations. This demonstrates a consistent spatial distribution pattern, with the highest dose in the posterior region, followed by the central area, and the lowest in the anterior region. This phenomenon occurs because the posterior bladder wall tends to be positioned closest to the radiation source, resulting in greater radiation energy absorption. While bladder filling provides relative dosimetric sparing for the anterior and central regions, it consequently increases the overall D2cc dose received by the bladder. The D2cc values for the bladder and rectum across the six bladder volume variations demonstrate that systematic increases in bladder volume affect the relative distance between the applicator and the bladder wall, directly impacting the received D2cc. The D2cc values for the bladder and rectum are presented in Table 1.

Table 1. D2cc Dose to the Bladder and Rectum at Variations in Bladder Volume

Bladder volume (cc)	D2cc Dose (cGy)	
	Bladder	Rectum
0	110	100
100	260	90
150	240	90
200	330	90

Bladder volume (cc)	D2cc Dose (cGy)	
	Bladder	Rectum
250	640	100
300	1080	100

An increase in bladder volume resulted in a highly significant rise in the bladder D2cc, from 110 cGy under empty conditions to 1080 cGy at a bladder volume of 300 cc. This pattern is consistent with anatomical principles, whereby bladder expansion pushes its walls, particularly the posterior region, closer to the radiation applicator, thereby exponentially increasing dose exposure in accordance with the inverse square law (Ab Shukor et al. 2022). Conversely, the rectal dose demonstrated remarkable stability (90-100 cGy), indicating that variations in bladder volume within this range have a minimal influence on the position or dose received by this OAR.

In general, the bladder D2cc increases, however, this increase is not linear and exhibits interesting behavior. An anomaly is observed at a volume of 150 cc, where the D2cc value decreases to 240 cGy from 260 cGy at 100 cc. This fluctuation may be caused by changes in the direction and nature of bladder deformation during the filling process. At specific volumes, bladder expansion may not predominantly push the posterior wall toward the applicator but instead expand superiorly or laterally, thereby slightly increasing the effective distance between the critical region and the radiation source. At volumes above 150 cc, a steep dose increase is observed, particularly between 250 cc and 300 cc (from 640 cGy to 1080 cGy). This surge indicates that bladder expansion positions the posterior region extremely close to the applicator beyond a certain critical point, resulting in a sharp dose escalation.

In this study, a bladder volume of 100 cc was identified as the optimal condition because it did not trigger an increase in dose to the rectum. This finding is consistent with the study by Mahantshetty et al. (2017), which reported that volumes of 50 cc and 100 cc were well tolerated and that adequate filling could be reproduced during cervical brachytherapy. Furthermore, their study also concluded that bladder filling did not significantly affect the DVH parameters of risk organs. However, the trend showed that larger volumes tended to receive higher absolute doses.

The stability of the rectal dose allows for flexibility in managing bladder volume. Conversely, the dose to the bladder is susceptible to changes in volume, necessitating a strict protocol (Hatanaka et al. 2016; Sharma et al. 2018). Simulations indicate that a bladder volume of approximately 100 cc is optimal, aligning with the findings of Mahantshetty et al. (2017), who reported that a bladder filling of 50–100 cc is well-tolerated and yields consistent volumes, making it a practical approach in clinical settings (Mahantshetty et al. 2017). In contrast, large volumes of 250–300 cc should be avoided due to the risk of significant bladder overdose. The results obtained in this study utilize a simplified phantom model. The anomalous result at 150 cc requires further investigation with a denser distribution of data points around this range to validate whether it represents a consistent pattern or a simulation artifact. Therefore, the D2cc dose was also calculated using an analytical method to cross-validate the experimental D2cc. Based on the quadratic regression analysis, the following equation was obtained:

$$\hat{Y}_i = 8{,}34 - 0{,}089X + 0{,}0003X^2 \quad (5)$$

The equation $\hat{Y}$ is used to determine the bladder D2cc value based on variations in bladder volume, as presented in Table 2.

Table 2. Comparison of Experimental and Analytical Bladder D2cc Doses

No.	Bladder volume (cc)	D2cc (Gy)	
		Experimental	Analytical
1.	100	2.6	2.4
2.	150	2.4	1.7
3.	200	3.3	2.5
4.	250	6.4	4.8
5.	300	10.8	8.6

The D2cc dose to the bladder demonstrates a model of increase corresponding to larger bladder volumes, which is evident in both the experimental results and the analytical calculations using quadratic regression. At smaller volumes (100–150 cc), the D2cc values remain relatively low. In contrast, a significant dose increase is observed at larger volumes (200–300 cc), reaching up to 10.8 Gy experimentally and 8.6 Gy analytically. Generally, the analytical results yield slightly lower dose values than the experimental findings. This discrepancy is likely attributable to the idealized assumptions inherent in the mathematical calculation, which do not account for tissue heterogeneity and the actual geometric conditions present in the experiment. Although a mean difference of approximately 1.1 Gy exists between the two sets of results, this deviation remains within acceptable tolerance limits. Consequently, the applied quadratic regression model can be considered sufficiently representative for describing the relationship between bladder volume and D2cc dose, both theoretically and clinically. Statistical analysis confirms that the quadratic regression model exhibits an excellent goodness-of-fit to the observational data, as indicated by a coefficient of determination (R^2) value of 0.92.

Optimizing bladder volume during high-dose-rate (HDR) intracavitary brachytherapy for cervical cancer is crucial for minimizing the radiation dose to organs at risk (OARs), specifically the bladder itself and the rectum. The reviewed studies provide valuable insights into the dosimetric effects of different bladder volumes and suggest optimal strategies for bladder management during treatment. A bladder volume of approximately 100 cc has been identified as a promising compromise. This volume appears to provide adequate dosimetric protection to the bladder by minimizing its dose exposure while maintaining a stable and low dose to the rectum. This stability in rectal dose offers some flexibility, but the high sensitivity of the bladder dose to its own volume necessitates a strict and consistent bladder preparation protocol. Conversely, large bladder volumes should be avoided, particularly those exceeding 250 cc. These volumes cause a significant anterior shift of the bladder, bringing a larger portion of its posterior wall closer to the radiation source. This leads to a steep and substantial increase in the bladder D2cc, heightening the risk of complications such as radiation cystitis. Therefore, implementing a controlled bladder filling protocol is an essential and practical clinical strategy to achieve an optimal balance between tumor control probability (TCP) and normal tissue complication probability (NTCP), ultimately enhancing the therapeutic ratio and improving patient outcomes.

The results of this study provide initial insights into the dynamics of bladder volume changes in response to dosage in the bladder and rectum, but require interpretation with consideration of several limitations that have not been thoroughly explored. Limitations include the use of a simplified phantom model with homogeneous materials. In addition, these findings are still preliminary because they are not supported by in vivo data or direct clinical validation, so their correlation with actual patient treatment outcomes requires further investigation.

CONCLUSION

The findings demonstrate that bladder volume is a parameter of paramount importance in HDR brachytherapy for cervical cancer, with a significant and direct impact on the bladder's own dosimetry, specifically on point doses and the D2cc. In contrast, the rectal D2cc remains remarkably stable and is largely unaffected by variations in bladder volume within the studied range. An optimal bladder volume of 100 cc was the most favorable compromise. This specific volume achieves the primary objective of significantly reducing the bladder D2cc, thereby directly mitigating the risk of bladder toxicity, while incurring only a negligible dosimetric effect on the rectum.

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