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Review Article

High Dose Rate Brachytherapy of Carcinoma of the Cervix: Applicability of Various Dosimetry Systems and Guidelines in the Dose Prescription and Treatment Planning

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Abstract

Purpose: This study is conducted to investigate applicability of various dosimetry systems and guidelines in the dose prescription and treatment planning of high dose rate brachytherapy of carcinoma of the cervix.

Material and Methods: Many dosimetry systems were devised to guide the treatment of carcinoma of the cervix. The Manchester system was the first one got wide acceptance among the radiotherapy centers Worldwide due to its reproducibility of dose specification and source distribution. The Manchester system is characterized by doses to points A and B, where dose is prescribed to point A. The definition of point A was modified time to time by different working groups to accommodate technological advancements. Another system recommended by the ICRU relates the dose distribution to the target volume rather than to specific points. The ICRU system for dose specification of brachytherapy for Ca.Cx. recommends an absorbed dose level of 60 Gy as a reference dose level for LDR treatments of the pear shaped 60 Gy isodose reference volume. For the combination of EBRT and ICBT, the reference isodose for ICBT is obtained by subtracting the EBRT dose from a total dose of 60 Gy. The source loading were similar in the ICRU system as that in the Manchester system, which includes entire uterus, cervix and vaginal mucosa. Both systems were effectively adopted for HDR brachytherapy with appropriate dose rate corrections. The ABS had presented guidelines for HDR brachytherapy of Ca.Cx. for CT or MRI based 3D treatment planning and dose delivery. For target contouring, ABS recommends the use of the Groupe European Curietherapie-European Society of Therapeutic Radiation Oncology (GEC-ESTRO) contouring guidelines for both CT and MRI based imaging, and the prescribed dose should cover 90% of the high - risk clinical tumor volume (HR-CTV).

Results and Discussion: Comparison of dose distributions of the Manchester / ICRU systems and ABS HR-CTV based dose prescriptions reveals entirely different area coverages. The Manchester / ICRU systems based dose prescriptions cover entire uterus which may have micro-invasive disease and at potential risk of recurrence in the uterus which does not cover in ABS HR-CTV based dose prescription, because the HR-CTV includes the cervix plus tumor extension at the time of brachytherapy, and 1 cm extension above the uterine vessels identified by intravenous contrast or the location where uterus begins to enlarge. On the other hand, there is a significant HR-CTV under coverage, for the patients of large pelvic region and over coverage for small pelvic region, when source loading and dose prescription is done based on the Manchester / ICRU systems. In one of our study, the dose prescription point is defined based on the anatomical variation of the pelvic cavity of the patients treated with HDR brachytherapy, which offers adequate coverage for cervix.

Conclusion: Every system or recommendations devised, so far, for HDR (or LDR) brachytherapy of carcinoma of the cervix, has negative and positive points in dose prescription and tumor coverage, or tumor contouring, which sometimes lead to tumor recurrence. Hence it is advice to the practicing radiation oncologist and brachytherapy physicist to consciously individualize the treatment for each patient.

Keywords: Brachytherapy; HR-CTV; HDR; ICRU

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Introduction

Incident of cervical cancer is low in developed nations but still is high in developing countries, where socio-economic factors play a major role not only in diagnosis but also in treatment. Locally advanced carcinoma of the cervix (Ca.Cx.) is treated with combination of External Beam Radiotherapy (EBRT) and intracavitary brachytherapy (ICBT), where ICBT is an important component of the treatment [1,2]. There are various dosimetry systems developed to guide implant procedure and dose prescription for Low Dose Rate (LDR), such as the Manchester Dosimetry System [3,4], and subsequently used in High Dose Rate (HDR) intracavitary brachytherapy for the treatment of Ca.Cx.

The HDR brachytherapy has advantages compared to LDR brachytherapy in terms of short outpatient treatment, comparable less associated toxicity, minimum applicator displacement during procedure and reduce radiation exposure to caregivers.

The Manchester Dosimetry System (MDS) is one of the most extensively used dosimetry system in clinics worldwide due to its simplicity and reproducibility. International Commission in Radiation Units & Measurements Report-38 (ICRU-38) discussed dose and volume specifications for reporting intracavitary brachytherapy and is widely accepted clinically [5]. With the advances in imaging technology and three dimensional (3D) treatment planning system, the dose prescription is shifting from point A to the clinical target volume (CTV) [6-10]. The new target for 3D image guided conformal treatments is for 90% of the high-risk clinical target volume (HR-CTV), is defined as D90, to receive at least the prescribed dose [7-10]. However, the Gynecological European Group of Curie-therapie and the European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) still recommend the recording of conventional point A doses during 3D-image based planning, at least for a transition period [7, 8].

This review article investigates the applicability of various dosimetry systems and guidelines in the dose prescription and treatment planning of high dose rate brachytherapy of carcinoma of the cervix, and compares with the American Brachytherapy Society (ABS) guidelines and recommendations (2012) [10].

Material and Methods

Many dosimetry systems were devised to guide the treatment of carcinoma of the cervix. The Manchester system was the first got wide acceptance among the radiotherapy centers Worldwide due to its reproducibility of dose specification and source distribution. The Manchester system is characterized by doses to points A and B, where dose is prescribed to point A. The definition of point A was modified time to time by different working groups to accommodate technological advancements. Another system recommended by the ICRU relates the dose distribution to the target volume rather than to specific points. The ICRU system for dose specification of brachytherapy for Ca.Cx. Recommends an absorbed dose level of 60 Gy as a reference dose for LDR treatments of the pear shaped 60 Gy isodose reference volume. For the combination of EBRT and ICBT, the reference isodose for ICBT is obtained by subtracting the EBRT dose from a total dose of 60 Gy. The source loading were similar in the ICRU system as that in the Manchester system, which includes entire uterus, cervix and vaginal mucosa. Both systems were effectively adopted for HDR brachytherapy with appropriate dose rate corrections. The ABS had presented guidelines for HDR brachytherapy of Ca.Cx. for CT or MRI based 3D treatment planning and dose delivery. For target contouring, ABS recommends the use of the GEC-ESTRO contouring guidelines for both CT and MRI based imaging, and the prescribed dose should cover 90% of the high - risk clinical tumor volume (HR-CTV).

(a) Manchester System

In the Manchester system (1938) [3], 1 to 3 radium tubes were placed in a rubber tube, which was inserted into the uterine canal. Simultaneously, radium tubes were loaded in appropriate-sized two ellipsoid rubber ovoids, with diameters 2, 2.5, and 3 cm, which were placed against the cervix and held at constant separation by a rubber spacer. No shielding was used in ovoids, so generous anteriorly and posteriorly packing was a requirement to reduce bladder and rectum doses. For dose prescription and reporting, the point A was originally defined as: draw a line connecting to the superior aspects of the vaginal ovoids and measuring 2 cm superior along the tandem and 2 cm perpendicular to this point and point B was to be 5 cm from the mid-line at the same level as point A. Ideally, point A represents the location where the uterine vessels cross the ureter. It is believed that the tolerance of these structures is the main limiting factor in the irradiation of the uterine cervix and point B represents dose to the lateral structures in the pelvis such as the obturator nodes.

Because of the inherent difficulty in visualizing the mucous membrane of the vagina, point A definition was revised in 1953 [4]. Point A was redefined by placement of its vertical origin at the external cervical os instead of the vaginal mucosa. Dose / dose rate to point A and point B changes depends on central tendon and ovoids loading pattern. The point A dose rate was approximately 0.53 Gy/hr for all allowed applicator loading patterns. Approximately 2/3 of the point A dose / dose rate contributed from the tandem and 1/3 from the ovoids. Point B dose / dose rate is typically 1/3, i.e. approximately 33%, of the point A dose / dose rate. The Manchester system specify maximum bladder and rectum point dose to be 80% or less than that of the dose to point A. If in any situation, the doses to the bladder and rectum are higher, the source loading should be altered in tandem and ovoids to achieve the goal.

(b) ICRU system

The ICRU has recommended a system of dose specification that relates the dose distribution to the target volume instead of the dose to a specific point. The dose is prescribed as the value of an isodose surface that just surrounds the target volume. The ICRU bladder point is localized by using a Foley catheter, with the balloon filled with a contrast material. On the AP radiograph, the bladder point is marked at the center of the balloon. On the lateral radiograph, the bladder point is the intersection of a vertical line drawn from the center of the balloon with the posterior surface of the balloon.

The rectal point is defined at the midpoint of the ovoid sources, or at the lower end of the intrauterine source, on the AP radiograph. On the lateral radiograph, it is located at 5 mm behind the posterior vaginal wall on a vertical line drawn from the middle of the ovoid sources. The posterior vaginal wall may be visualized by using radiopaque gauze for the vaginal packing.

The reference volume is the volume of 60 Gy isodose surface that just surrounds the target volume. Both dose and reference are recommended to be in the patients record.

(c) GYN GEC-ESTRO guidelines

The Groupe Europeen Curietherapie-European Society of Therapeutic Radiation Oncology (GEC-ESTRO) presented guidelines to support 3D imaging based 3D treatment planning approach in cervix cancer brachytherapy [7,8]. It is recommended to use CT and/or MRI compatible applicators that allow a sectional image based approach to assess the gross tumor volume (GTV), clinical target volume (CTV) and organs at risk (OARs). Dose prescription is defined to a target volume not to point A, however, it's recommended to document conventional point A dose.

MRI is preferred for target localization and volume delineation. In general, most patients are treated with combination of EBRT and BT so GTV changes at diagnosis, during and at the end of EBRT. Target definition recommended 2 CTV approach; a first target related to the extent of GTV at diagnosis should include the intermediate risk clinical target volume (IR-CTV) and a dose of 60 Gy should be prescribed to this target volume. A second target related to the extent of GTV at time of initiating brachytherapy, which should be defined taking into account tumor extent at diagnosis and must be considered high risk clinical target volume (HR-CTV), and a dose of 80 – 90 Gy should be given to this target. This high dose is considered sufficient enough to sterilize macroscopic tumor cells.

The HR-CTV covers residual macroscopic tumor and microscopic cancer cells that includes whole cervix and extra-cervical tumor extension. The IR-CTV covers initial macroscopic extent of tumor, microscopic extension plus margins. Tumor margins varies from 5 mm to 15 mm around IR-CTV / HR-CTV according to potential tumor spread and tolerance of OARs. The OARs includes rectum, bladder, sigmoid colon and vagina. GEC-ESTRO guidelines specify to record doses to target volumes (IR-CTV and HR-CTV) and OARs. D90 and D100 should be documented for HR-CTV along with doses to point A, and ICRU rectum and bladder points. For OAR; D0.1cc, D1cc, D2cc, if volumes are delineated; or D5cc, D10cc, if walls are contoured, should be recorded.

(d) ABS 2012 guidelines

ABS revised it's 2000 recommendations in 2012 [11]. The new recommendations address image-guided treatment planning and delivery, and recommended reporting parameters for quality assurance [10]. The ABS 2012 also recommends adoption of the GEC-ESTRO guidelines for contouring, image-based treatment planning, and dose reporting [8,9]. CT and MRI based localization allows for correlation of anatomic data in respect to radioactive source positioning. Volume based dosimetry should be performed and D90, D100 and V100 should be recorded for HR-CTV. D0.1cc and D2cc is recorded for OARs, for volume delineation, and D5cc, for organ wall contouring [9].

HR-CTV includes the width of cervix plus any parametrial extension. The superior border of the cervix should extend at least 1 cm above uterine vessels identified by IV contrast or location where uterus begins to enlarge. If cervix can't be identified in CT images, approximate 3 cm height should be contoured for cervix, with the caveat for CT based planning to treat entire length of tandem. CT/MRI compatible applicator should be used and type of applicator should be recorded.

Volume based dosimetry should be performed and D90, D100 and V100 should be recorded for HR-CTV. D0.1cc and D2cc are recorded for OARs, for volume delineation, and D5cc, for organ wall contouring [9]. Doses to point A, and ICRU rectal and bladder points should also be reported.

Issues with these Systems

a. Limitations of point A

Point A is an applicator related point that does not specify anatomical structures. Dose to point A is very sensitive to the position of the ovoid sources relative to the tandem sources, which should not be the determining factor in deciding on implant duration. Depending upon the size of the cervix, point A may lie inside or outside of the cervix (Figure 1). Thus, dose prescription to point A could risk under dosage of large cervical cancers or over dosage of small ones. Wide variation in point A, in respect to the ovoids, point A often occurs in a high-gradient region of the isodose distribution. Therefore, minor differences in position can result in large differences in dose. Anderson et al., (2012) reported significant variations in point A locations (mean: 0.5 cm, maximum: 2.1 cm, $p < 0.001$) with patient's anatomy.

b. Limitations with ICRU system

ICRU 38 report defines the concept of the reference volume of 60 Gy absorbed dose prescription, because point A and point B definitions are interpreted differently among radiation oncologists and radiation oncology centers. But again the concept of 60 Gy was defined differently by different users in same or in different centers. Another weakness of the system is the inability to visualize the target volume. In the evaluation, ICRU dimensions of maximum width, height, and thickness of intracavitary implant regions may not be clearly identified/recognized. However if entire intracavitary surface is evaluated, the regions of under dose can be identified and addressed.

OAR Reference ICRU Points

ICRU bladder and rectum reference points are not true representative of that receive high dose. The bladder and rectal doses in ICRU reference points were significantly underestimated when compared with bladder D2cc and rectum D2cc doses, respectively [12]. In an study conducted by Passi et al., (2009) [13] reported that there was no correlation between maximum dose to bladder and rectum and dose to ICRU Bladder and ICRU Rectal points, and also no correlation could be established between the doses to nodal metastasis and the doses received by trapezoid points.

Issues with ABS 2012 guidelines

ABS point A and point B have same drawbacks as was with the Manchester system and the ICRU point A and point B. As discussed in foregoing section, that point A is not related to patient's anatomy and is not often in paracervical triangle, which is not a reliable indicator of minimum tumor dose. Point A is often in the region of steep dose gradient and is sensitive to applicator displacement during treatment and also, varies on applicator type. Similarly point B does not always represent obturator nodes. Points A and B can only be defined

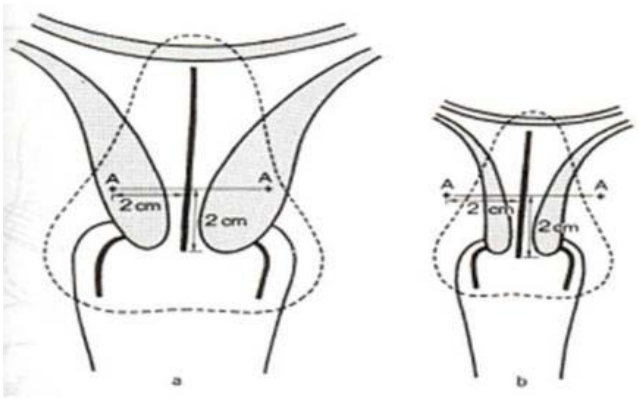

Figure 1: Depending upon the size of the cervix, point A may lie inside or outside of the cervix.

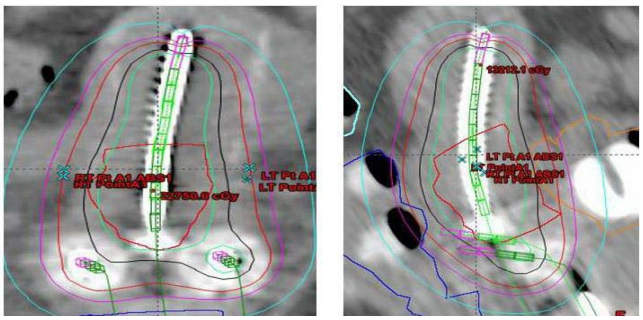

Figure 2: If Manchester loading is done the HR-CTV is covered with adequately coverage of uterine body.

accurately for fixed applicator geometry configurations. Noguchi et al., (1988) [14] studied the incidence of invasion of the carcinoma of the cervix to the uterine body in 301 cases, reported that 21.6% cases had invasion of the disease to the uterine body. They also reported the incidence according to the stage of the disease, such as 7.8% in stage Ib, 25.5% in stage IIa, 38.2% in stage IIb. The vaginal wall invasion was in 58.5% of all positive cases, the parametrial infiltration in 87.7%, and pelvic lymph node metastasis in 52.3% cases. It is obvious that the CT images fails to provide adequate information of invasion of microscopic tumor cells as compare to MR images. Therefore, If CT bases contouring of HR-CTV is done then it does not adequately cover the uterine body where tumor extension and clearly underdoge the uterine body of possible microscopy invasion.

Results & Discussion

Comparison of dose distributions of Manchester / ICRU systems and ABS HR-CTV based dose prescriptions reveals entirely different area coverage. The Manchester / ICRU systems based dose prescriptions cover entire uterus which may have micro-invasive disease and at potential risk of recurrence in the uterus which does not cover in ABS HR-CTV based dose prescription, because the HR-CTV includes the cervix plus tumor extension at the time of brachytherapy, and 1 cm extension above the uterine vessels identified by intravenous contrast or the location where uterus begins to enlarge. On the other hand, there is a significant HR-CTV under coverage, for the patients of large pelvic region and over coverage for small pelvic region. If the Manchester loading is done the HR-CTV is covered with adequately

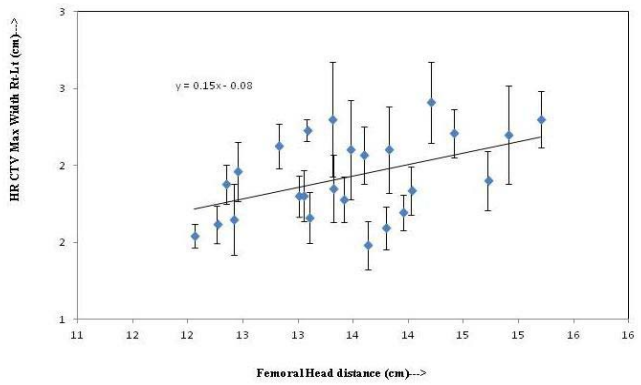

Figure 3: Plot between femoral heads distance and max one-half width of HR-CTV.

coverage of uterine body as shown in (Figure 2).

In one of our study [15], the dose prescription point is defined based on the anatomical variation of the pelvic cavity of the patients treated with HDR brachytherapy. The location on the dose prescription point was defined using least square best fit between HR - CTV width (in the left - right dimension) and femoral head distance / pelvic cavity width, obtained from 125 retrospective HDR treatment plans (Figures 3 and 4). For testing the reliability of this point for dose prescription in the HDR intracavitary brachytherapy of carcinoma of the cervix, the HR-CTV coverage is examined and demonstrate adequate coverage for cervix and uterine body for the equivalent Manchester System loadings.

The newly defined dose prescription point, hereinafter called point A, is defined at the same level as was in the Manchester System, based on applicator coordinates, can be given by the correlations

Point A based on distance between femoral heads:

$$A\ (cm) = 0.15 \times (\text{R-L dist. between Fem. Heads in cm}) - 0.08 \quad (1)$$

Point A based on dimension of maximum pelvic cavity widths:

$$A\ (cm) = 0.17 \times (\text{Max Pelvic Cavity width in cm}) - 0.03 \quad (2)$$

These relations give fairly appropriate location of point A, which provides adequate coverage to the HR - CTV compared to the point A defined based on applicator coordinates.

The cavity width measurements at maximum dimension are subjective and may have variation from patient to patient, while the femoral head distance measurements are reproducible and can be measured with least variation. Hence, the point A defined based on femoral head distance would be an appropriate tool to use for dose prescription.

Conclusion

Every system or recommendations devised, so far, for HDR (or LDR) brachytherapy of carcinoma of the cervix, has negative and positive points in dose prescription and tumor coverage, or tumor contouring, which sometimes lead to tumor recurrence.

Systems that have target volume contouring based on MRI

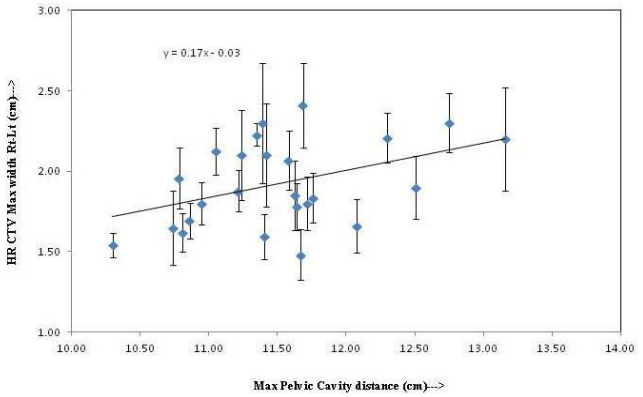

Figure 4: Plot between max pelvic cavity distance and one-half width of HR-CTV.

enables to provide adequate irradiation of the diseases. High chances of inadequate dosing are there in CT based contouring and planning. ABS system which involved CT based planning does not offer better tumor coverage than Traditional system, such as Manchester system.

Hence it is advice to the practicing radiation oncologist and brachytherapy physicist to consciously individualize the treatment for each patient.

References

1. Klopp A, Eifel P, Chemoradiotherapy for cervical cancer in 2010. Curr Oncol Rep 2011; 13; 77-85.
2. Monk B, Tewari K, Koh W. Multimodality therapy for locally advanced cervical carcinoma: State of the art and future directions. J Clin Oncol 2007; 25: 2952-2965.
3. Tod M and Meredith W. A dosage system for use in the treatment of cancer of the uterine cervix. Br J Radiol. 1938, 11: 809–824.
4. Tod M, Meredith WJ. Treatment of cancer of the cervix uteri, a revised Manchester method. Br J Radiol. 1953; 26: 252–257.
5. ICRU report 38. Bethesda, MD: International Commission on Radiation Units and Measurements; 1985; 1-20.
6. Kirisits C, Potter R, Lang S et al. Dose and volume parameters for MRI-based treatment planning in intracavitary brachythe -rapy for cervical cancer. Int J Radiat Oncol Biol Phys 2005; 62: 901-911.
7. Potter R, Haie-Meder C, Van Limbergen E et al. Recommendations from gynaecological (GYN) GEC ESTRO working group (II): concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy-3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. Radiotherapy and Oncology 2006; 78: 67-77.
8. C. Haie-Meder, Pötter R, Van Limbergen E, Briot E, De Brabandere M, Dimopoulos J, et al. Recommendations from gynaecological (GYN) GEC ESTRO working group (I): concepts and terms in 3D image-based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. Radiotherapy and Oncology 2005; 74: 235-245.
9. Viswanathan AN, Erickson BA. Three-dimensional imaging in gynecologic brachytherapy: A survey of the American Brachytherapy Society. Int J Radiat Oncol Biol Phys 2010; 76: 104-109.
10. Viswanathan AN, Thomadsen B. American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part I: General principles. Brachytherapy 2012; 11: 33-46.
11. Nag S, Erickson B, Thomadsen B, Orton C, Demanes JD, Petereit D. The American Brachytherapy Society recommendations for high dose rate brachytherapy for carcinoma of the cervix. Int J Radiat Oncol Biol Phys 2000; 48: 201-211.
12. Chottaweesak P, Shotelersuk K, Amornavichet N, Khorprasert C, Oonsiri P. Comparison of bladder and rectal doses between conventional 2D and 3D brachytherapy treatment planning in cervical cancer. Biological Imaging and Intervention Journal 2014; 10: 1-7.
13. Passi K, Kehwar TS, Vashistha R, Singh B, Jain V, Gupta SJ. High-dose-rate brachytherapy with external beam radiotherapy in the treatment of carcinoma of cervix: dosimetric and radiobiologic analysis. Journal of Radiotherapy in Practice 2009; 8: 215-227.
14. Noguchi H, Shiozawa I, Kitahara T, et al. Uterine body invasion of carcinoma of the uterine cervix as seen from surgical specimens. Gynecol Oncol 1988; 30:173-182.
15. Goyal MK, Rai DV, Kehwar TS, Manjhi J, Heintz BH, Shide KL, et al., Can the study of three-dimensional volumetric imaging further refine and simplify high-dose-rate (HDR) intracavitary brachytherapy dose prescription when treating cervical cancer using limited resources?. Applied Clin Med Phys, 2016.

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