Reports of Practical Oncology and Radiotherapy 25 (2020) 851–855

Available online at www.sciencedirect.com

Reports of Practical Oncology and Radiotherapy

journal homepage: http://www.elsevier.com/locate/rpor

Original research article

Dosimetric comparison of manual forward planning with uniform dwell times versus volume-based inverse planning in interstitial brachytherapy of cervical malignancies

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ARTICLE INFO

Article history:
Received 26 March 2020
Received in revised form 31 May 2020
Accepted 12 August 2020
Available online 11 September 2020

Keywords:
Manual forward planning
Inverse optimization
Interstitial brachytherapy
Brachytherapy indices

ABSTRACT

Aim: Dosimetic comparison of manual forward planning(MFP) with inverse planning(IP) for interstitial brachytherapy(ISBT) in cervical carcinoma.
Background: Brachytherapy planning by MFP is more reliable but time-consuming method, whereas IP has been explored more often for its ease and rapidness. The superiority of either is yet to be established.
Methodology: Two plans were created on data sets of 24 patients of cervical carcinoma who had undergone ISBT, one by MFP with uniform dwell times and another IP on BrachyVision 13.7 planning system with a dose prescription of 600 cGy. Isodose shaper was used for improving conformity & homogeneity. Dosimetric parameters for target and organs at risk (OARs) were recorded. Conformity index (COIN), dose homogeneity index (DHI), overdose index (OI), Coverage index (CI) and dose nonuniformity ratio (DNR) were calculated.
Results: Mean high risk clinical target volume: 73.05(±20.7)cc, D90: 5.51 Gy vs. 5.6 Gy ($p = 0.017$), V100: 81.77 % vs. 83.74 % ($p = 0.002$), V150: 21.7 % vs. 24.93 % ($p = 0.002$), V200: 6.3 % vs. 6.4 % ($p = 0.75$) for IP and MFP, respectively. CI: 0.81(IP) and 0.83(MFP) ($p = 0.003$); however, COIN was 0.79 for both plans. D2cc of OARs was statistically better with IP (bladder 54.7 % vs. 56.1 %, $p = 0.03$; rectum 63 % vs. 64.7 %, ($p = 0.0008$).
Conclusion: Both MFP and IP are equally acceptable dosimetrically. With higher dose achieved to the target, for a similar OAR dose, MFP provides greater user flexibility of dwell positions within the target as well as better optimization. Isodose shaper may be carefully used for fine tuning. Larger sample sizes and clinical correlation will better answer the superiority of one over the other.

1. Introduction

External beam Radiotherapy (EBRT) followed by brachytherapy (BT) is the standard of care and an integral part of local control for cervical carcinoma. Patients with large volume residual disease post EBRT or with suboptimal anatomy pose a challenge for routine Intracavitory Brachytherapy (ICBT); hence, Interstitial Brachytherapy (ISBT) or a combination of intracavitary and interstitial brachytherapy (IC + ISBT) is recommended. Some centers choose to boost the residual disease using Intensity Modulated Radiotherapy (IMRT)/ Stereotactic Body Radiotherapy (SBRT) when brachytherapy is not feasible for various reasons. However, brachytherapy contributes to the improvement of local control and overall survival by delivering the intended high dose to the disease in the most conformal manner with maximal sparing of Organs at risk (OARs), and thus remains the standard of care.[1,2]

Template based ISBT has gained widespread popularity with the advent of 3D image-based planning. Imaging with Computerized Tomography (CT)/ magnetic resonance imaging (MRI) helps in better visualization of the gross tumor as well as the essential organs to be spared. This in turn translates into better planning and optimization techniques.

Of the various planning and optimization methods available for brachytherapy, the basic premise is to deliver a high radiation dose to tumor volume and to spare the surrounding normal tissues to

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https://doi.org/10.1016/j.rpor.2020.08.005
1507-1367/

the maximal capacity, offering the best possible therapeutic ratio.[3] A literature search revealed a frequent use of volume based inverse planning method for ISBT.[4,5]

Traditionally, orthogonal x-rays have been used to plan brachytherapy treatments with the Paris Dosimetry system, even for multiplanar implants. This did not permit for isodose and dwell time manipulations in accordance with volumes under consideration and only a standard plan could be delivered based on implant geometry for temporary interstitial implants with uniform dwell times, even if it meant high doses to the surrounding normal tissues. At present, with the advent of 3D-image based brachytherapy planning system, it is possible to accurately delineate the volume with major risk of local recurrence owing to the residual macroscopic disease, i.e. high-risk Clinical Target Volume (HRCTV), and alter the dwell positions to suit the coverage of the HRCTV and limit doses to OARs. Various methods of forward planning have been in use, such as manual loading of dwell positions based on the tumor volume, uniform loading of all dwell times followed by optimization of the same, dose point optimization, etc.[6,7] However, these are thought to be time consuming and inverse planning is favoured in many set-ups, especially for multiplanar interstitial implants.

In brachytherapy inverse planning, the system automatically selects the active dwell positions from all possible dwell locations for the specified target volume and then determines dwell times that come close to meeting the clinician's dose prescription.[8,9] This results in unfavorably large high dose volumes, especially in the case of non-ideal implants where the desired spatial geometry of the implant could not be achieved. Though heterogeneity is an inherent and desirable property in BT, it is beneficial only if these hot spots lie within the tumor and minimum tumor dose (MTD) at the periphery. This can only be done by manual iterations even after inverse planning.[5]

Despite being the fourth most common malignancy among women, especially in low- and middle-income nations, the optimal method of planning and optimization in template based ISBT is not standardized yet in gynaecological malignancies and planning recommendations are lacking. There is a scope for further research in this area to define a better method of planning. This study is an attempt for the same and is presented as an institutional experience of a tertiary cancer centre.

2. Aims and objectives

To compare the volume-based inverse planning and forward planning in interstitial brachytherapy of cervical malignancies in terms of dosimetric parameters by generating two different plans in the same patient.

3. Materials and methods

Data sets of twenty-four patients with histologically proven carcinoma cervix treated with template based ISBT from January to July 2019 were chosen for the study. All these patients had completed external beam radiotherapy by 3D Conformal Radiotherapy to a dose of 4500–5000 cGy before undergoing ISBT. By institutional protocols, patients with a significant residual disease destroying the cervical anatomy, where the uterus could not be sounded, were subjected to pure ISBT with Syed-Neblett template and needles only. The target volumes including HRCTV, intermediate risk CTV (IR-CTV) and the rectum and bladder were delineated on the CT scan using the clinical findings both prior to EBRT and the findings at Examination Under Anaesthesia (EUA) at the time of BT in accordance with the Groupe European de Curietherapie- European Society for Radiotherapy and Oncology (GEC ESTRO) guidelines.[10] Owing to the logistic difficulties of a high volume regional cancer centre, MRI is not done routinely at our institution. Thus, gross tumor volume was not delineated and plans were evaluated only based on HRCTV. Brachy-vision version 13.7 software for single Iridium-192 stepping source with an inherent step size of 0.5 cm was used. A dose of 600 cGy was prescribed and two separate plans were generated on the images for four fractions.

3.1. Inverse planning method (IP)

Inverse Planning was performed using the adaptive volume optimization algorithm which utilizes the input data of the user defined dosimetric constraints on the surface of the target and OAR to generate the optimal dwell time distribution corresponding to the dwell positions on the applicator befitting the HRCTV. The following criteria were used for planning: HRCTV D90 (dose received by 90 % of the target volume) to receive > 95 % of the prescribed dose and a minimum of 90 % of prescribed dose; D2cc (the most irradiated 2cc volume) of the bladder, rectum, and sigmoid to receive less than 70 % of the prescribed dose. V150 % and V200 %, target volume receiving 150 % and 200 % of the dose, respectively, were limited to be within 30 % and 10 % as an institutional protocol. Isodose shaper was used upon the above-generated plan to limit the spillage of 200 % isodoses beyond the needles.

3.2. Manual forward planning method (MFP)

In this method, after the catheters were reconstructed, the portion of each catheter lying within the target volume was uniformly loaded with source dwell positions starting from the first slice to the last slice of contours individually. The dose was prescribed and dwell positions of all catheters loaded to equal dwell times ranging from 1.5 to 2.5 s depending upon needle positions. Further adjustments of dwell times were made to reduce the high dose areas. Fine tuning of the isodoses was done using the isodose shaper.

Both plans were accepted with a minimum requirement of at least D90 of 90 % or more. The dosimetric parameters of both plans were collected which included:

D90: defined as the dose received by 90 % of the target volume.

V100 of CTV: defined as the percentage of target volume receiving 100 % of dose.

V150 of CTV: defined as the percentage of target volume receiving 150 % of dose.

V200 of CTV: defined as the percentage of target volume receiving 200 % of dose.

TV- is the Target Volume

TVD_{ref} - is the reference target volume (taken as volume receiving 100 % of the prescribed dose for all calculations)

$TV_{1.5ref}$ – is the volume receiving 1.5 times the prescribed dose.

TV_{2ref} - is the volume receiving 2 times the prescribed dose.

V_{ref} – volume receiving 100 % of the prescribed dose irrespective of the target delineated (derived by generating an isostructure of volume receiving 100 % dose)

Also, the D2cc (minimum dose received by the most irradiated part) of the bladder and rectum were documented for comparison. The GEC-ESTRO recommended indices for interstitial brachytherapy were calculated using the following method for the objective assessment and comparison of the plans.[11–14]

1. Coverage Index (CI): CI is the fraction of the Target Volume (TV) that receives the prescribed dose. This index gives an estimate of how much of the target received 100 % of the dose. In ideal condition, CI is 1.

$$\text{Coverage Index (CI)} : \frac{TVDref}{TV} \quad (1)$$

2. Dose homogeneity index (DHI): DHI is the ratio of the TV receiving a dose, approximately 1.0–1.5 times of the reference dose,

Table 1
Dose volume parameters for inverse and forward planning.

Parameters (Mean)	Inverse plan Mean (SD)	Forward plan Mean (SD)	P value
D90 (Gy)	5.51 (±0.23)	5.6 (±0.16)	**0.017***
V100 (%)	81.77 (±3.62)	83.74 (±2.59)	**0.002***
V150(%)	21.77 (±4.19)	24.93 (±5.06)	**0.002***
V200(%)	6.29 (±1.68)	6.41 (±1.89)	0.759
CI	0.81 (±0.04)	0.83 (±0.03)	**0.003***
DHI	0.73 (±0.04)	0.7 (±0.05)	**0.007***
OI	0.076 (±0.02)	0.071 (±0.02)	0.313
DNR	0.26 (±0.04)	0.29 (±0.05)	**0.006***
COIN	0.79 (±0.04)	0.79 (±0.04)	>0.999
D2cc Bladder (%)	54.78 (±13.2)	56.13 (±12.6)	**0.034***
D2cc Rectum (%)	63.06 (±6.09)	64.71 (±5.31)	**0.001***

SD- Standard Deviation, $p < 0.05$ statistically significant.
D90- dose received by 90 % of the target; V100- volume of target receiving 100 % of the prescribed dose; V150- volume of target receiving 150 % of the prescribed dose, V200- volume of target receiving 200 % of the prescribed dose; CI- Coverage Index; DHI- Dose homogeneity index; OI- Overdose index; DNR- Dose nonuniformity index; COIN-Conformity index, D2cc bladder- minimum dose to most irradiated 2cc of bladder; D2cc rectum- minimum dose to most irradiated 2cc of rectum.

to the volume of the target that receives a dose equal to or greater than the reference dose.[15] In ideal condition the DHI is 1.

$$\text{Dose homogeneity index (DHI)}: \frac{TVDref - TV1.5ref}{TVDref} \quad (2)$$

3. Overdose volume index (OI): This is the ratio of the TV which receives a dose ≥2.0 times of the reference dose tothe volume of the target that receives a dose equal to the reference dose. In ideal condition the OI is 0.

$$\text{Overdose volume index (OI)}: \frac{TV2ref}{TVref} \quad (3)$$

4. Dose non-uniformity ratio (DNR): This is the ratio of the TV which receives a dose equal to or greater than 1.5 times of the reference dose to the volume of the target which receives a dose equal to the reference dose.[16] In ideal condition the DNR is 0.

$$\text{Dose non-uniformity ratio (DNR)}: \frac{TV1.5ref}{TVref} \quad (4)$$

5. Conformity Index (COIN): COIN describes how well the reference dose encompasses the TV and excludes non-target structures. The fraction of the TV which is covered by the reference dose is described by c_1 and the fraction of the total volume covered by the reference dose that belongs to the TV by c_2.[17] In ideal condition the COIN is 1.

Conformity Index (COIN): $c_1 \times c_2$

$$\text{Where c1 is given by } \frac{TVDref}{TV} \text{ and c2 is given by } \frac{TVref}{Vref} \quad (5)$$

6. Both plans were assessed and compared using the above-mentioned parameters and indices. Statistical analysis of the dose parameters of both sets of plans was done with the help of student's paired t-test for a significance level of 0.05.

4. Results

A total of 24 patients data sets were planned by manual forward with equal dwell times and volume based inverse planning. D90, V100, V150, V200, D2cc of the bladder and rectum were recorded for calculating the various indices and compared for both plans. The mean volume of CTV was 73.05(±20.7) cc. The various other dose volume parameters and indices were as given in Table 1. The D90 (p=0.017) and V100 ($p = 0.002$) were found to be significantly better in forward planning (Fig. 1), whereas the high dose volume namely V150 ($p = 0.002$) was better in inverse planning.

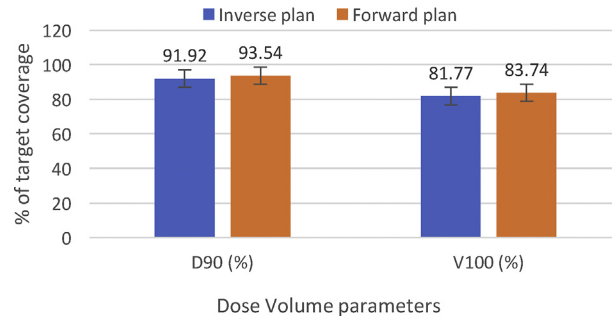

Fig. 1. The D90(%) and V100(%) for inverse and forward planning: D90- dose received by 90 % of target volume in percentage; V100- volume of target receiving 100 % of the prescribed dose.

Among the various dose volume indices calculated, the coverage index ($p = 0.003$) favoured the forward planning whereas the dose homogeneity index ($p = 0.007$) and dose non-uniformity ratio ($p = 0.006$) favoured the inverse planning (Fig. 2). The conformity was identical for both the plans. The doses to both rectum and bladder were better achieved with inverse planning though both were within tolerance limits of the organs.

5. Discussion

Multiple optimization techniques have been discussed for interstitial implants. However, we lack evidence to suggest a better technique and adequacy of optimization of any plan. There are few studies reporting a comparison of optimization using Inverse Planning by Simulated Annealing (IPSA) versus manual optimization in Gynaecological interstitial brachytherapy.[13]

The present study was an attempt to reintroduce the simplicity of uniform dwell times of the Paris Dosimetry system aided with the present sophisticated planning and calculation methods available to ease the process of planning with better reliability.

Dose optimization is imperative to be able to deliver the intended high dose to the high-risk clinical target volume and to restrict the doses to the OARs. An optimum application with the use of 16–22 needles has been attempted in the present study. Karouzakis et al.[18] have reported that an increase in the number of catheters may lead to an increase in the number of negative dwells, which impairs the quality of the plan. They suggest that inverse planning may allow the usage of a reduced number of catheters, without affecting the dose distribution. However, optimization cannot be used to compensate for an inferior application.

Bondel et al.[19] have compared geometric optimization versus volume optimization with and without the use of additional graphical optimization. They have performed geometric optimization using dose points placed within the HRCTV and normalization done to the same. Inverse planning has been done using a lower objective of 95 % and upper objective of 125 % to the target, with maximum dose to the rectum and bladder set at 60 %. While the inverse planning has used similar objectives in the current study, the forward planning has been performed using the uniform dwell time optimization to start with. Jamema et al.,[20] Mohit et al.[21] and Choi CH et al.[22] have demonstrated the use of graphical optimization upon an inverse plan for ISBT in carcinoma of the prostate, cervix and tongue respectively. Isodose shaper has been similarly used in the current study for inverse and forward planning methods with minimal adjustments to manually modify the conformity and homogeneity of the doses.

The quality of the treatment plans enables us to evaluate the performance of the different optimization models. Dewitt et al.[23] have observed a significant reduction in the doses to the OARs with no significant improvement in the target coverage with use of inverse

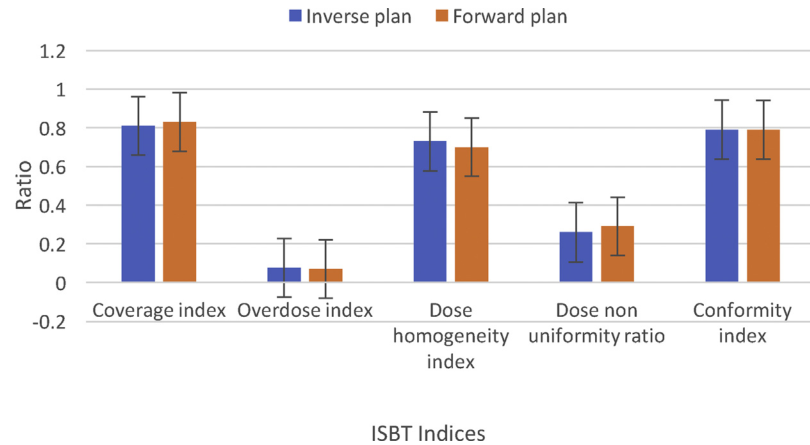

Fig. 2. Comparison of various brachytherapy dose volume indices for ISBT (Interstitial Brachytherapy).

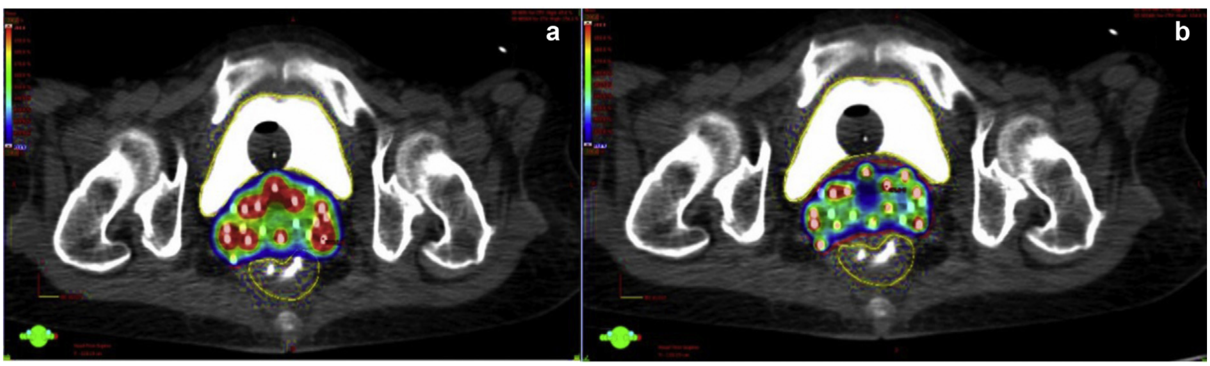

Fig. 3. Comparison of inverse and forward plan in a single patient CT image. (3a) Inverse plan without graphical optimisation, system generated plan with bulging of high dose volumes within the target so as to give 100 % target coverage, (3b) Inverse plan with Graphical optimisation. Isodose shaping can reduce the high dose volumes within the target with acceptable target coverage. Isodose wash red-200 % dose and blue-100 % dose in the figure.

planning. Kannan et al.[24] and Trnkova et al.[25] have demonstrated that inverse planning was superior in terms of HRCTV coverage and homogeneity. In our study the HRCTV coverage was better with forward planning whereas OARs were spared to a greater degree with inverse planning.

The mean CTV in the current study was 73.05(±20.7) cc in comparison with others ranging from 58cc – 137cc, which basically depends on the predominant stage at presentation and the volume of residual disease at brachytherapy. In the present study, manual optimization has achieved a higher mean D90 and V100 than inverse planning, the difference being statistically significant. In contrast, Kannan et al.[24] achieved a higher mean D90 with inverse planning. This could have been at the cost of a higher inhomogeneity within the target. Bondel et al.[19] obtained better V100 with Geometric manual optimization with dose shaping in comparison with volume optimization (88.11 % vs. 86.11 %). The Coverage Index in the current study is 0.81 for an inverse plan and 0.83 for a forward plan (p = 0.003). This is in the lower range of what is reported in literature, maybe because of a greater emphasis given to achieving homogeneity. The COIN was, however, identical in both inverse and forward plans at 0.79±0.04, which is similar to the study by Sharma et al.[26]

In comparison with DHI reported in previous studies, a better DHI has been achieved in the current study, which could be attributed to the carefully used graphical optimization for fine adjustment. However, if not further optimized graphically, inverse planning generated large volumes of 150 % and 200 %. It was also observed that in inverse plans much time was spent on reducing the high dose volumes during graphical optimization as opposed to the forward plan (Fig. 3 & 4). The impact of high dose volumes which may result in tissue necrosis have been less commonly reported in clinic with regard to different planning techniques.

Inverse planning is assumed to be less time consuming in comparison with forward planning and has, hence, being extensively explored as a choice.[20,21,24,25] However, it was observed that the source loading in the peripheries of the target volume in the inverse plan is sparse, especially when the implant was less than ideal, the D90 coverage was inadequate with larger high dose volumes and large variations with respect to dwell times.[22,27] In a forward plan, dwell positions are manually loaded and adjusted wherever required, though time consuming and laborious, provided flexibility for better optimization.

Post optimization, the V200 was small and limited to the needles alone and the OI was 0.07 in both techniques, which was within the limits of 0.08 found in other studies.[13] The doses achieved to D2cc of the rectum and bladder were found to be lesser with inverse planning.

The drawbacks of the current study are a relatively small sample size and failure to record the time required to create each plan. However, this is only a dosimetric study which is based on evaluation of Dose Volume Histogram (DVH) parameters and indices and does not take into account other factors like fraction size; number of fractions; elapsed treatment duration (gap between the days); spatial information for locating the hot and cold spots; internal organ motion and deformation leading to significant variation in volume delineation, all of which may result in varying clinical outcome.

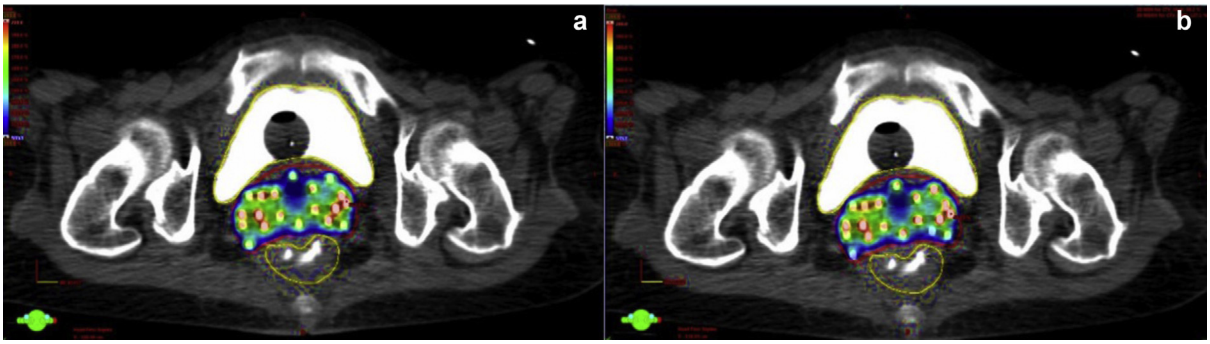

Fig. 4. Comparison of inverse and forward plan in a single patient CT image. (4a) Forward plan with uniform loading of dwell times, (4b) Forward plan with Graphical optimization, shows minimal requirement of isodose shaping to the initial plan with acceptable target coverage and restriction of 200 % doses to within the needles. Isodose wash red-200 % dose and blue-100 % dose in the figure.

6. Conclusion

Both MFP and IP are equally acceptable dosimetrically. With higher dose achieved to the target, for a similar dose to the OARs, MFP provides greater user flexibility with respect to dwell positions within the target as well as for better optimization. Isodose shaper is an important optimization tool which may be carefully used for fine tuning. IP is extensively studied unlike MFP in the era of 3D-image based BT; hence, larger sample sizes and clinical correlation will better answer the superiority of one over the other.

Conflict of interest

None Declared.

Financial statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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