***Proceedings Article***

# On-line and off-line correction strategies using megavoltage computed tomography in prostate cancer helical tomotherapy

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***SUMMARY:*** *At our Institution around 200 patients were treated for prostate cancer with helical tomotherapy (HT) in the last two years. MVCT was routinely used to correct patient/tumour positioning. For adjuvant treatments the study reports our experience in the application of on- and off-line set-up correction strategies in order to modelling and to assess the optimal off-line strategies to reduce set-up errors: data on 36 patients were analyzed. For radically treated patients, daily on-line correction with "prostate" matching is routinely performed and the data of 21 patients concerning daily correction taking both organ motion and set-up into account were analyzed. Before assessing the organ motion component, an investigation about inter-observer variability in tracking the prostate through direct MVCT visualization was also considered.*
*In summary, using MVCT during the first week of the treatment with an action level equal to 3 mm was found to be effective in significantly reducing systematic set-up error for adjuvant prostate treatment; the estimate of the residual error from the on-line correction strategy analysis suggests that the application of an off-line protocol with systematic set-up correction after the first 4 sessions without any action level may further reduce the residual systematic error below or around 1.5 mm (1 SD). Compared to such off-line approach, the additional improvement of on-line correction does not seem to be clinically relevant; off-line correction strategies for set-up correction with HT may reasonably replace on-line correction with a large sparing of time and resources.*
*Concerning "prostate" registration, a small inter-user variability registration was found probably due to a relatively small impact of organ motion depending on the rectal emptying procedures routinely performed. The same result was confirmed by the small difference estimated between planning and therapy position through an automatic bone matching and then by the manually adjustment of the physician trough direct visualization of prostate.*

***KEYWORD:*** *Helical tomotherapy, Prostate cancer, Set-up and organ motion modelling.*

## Strategie di correzione on-line e off-line con la megavoltage computed tomography nella tomoterapia elicoidale per i carcinomi prostatici

***RIASSUNTO:*** *Nel nostro Istituto negli ultimi due anni sono stati trattati con l'unità di tomoterapia elicoidale (HT) circa 200 pazienti per carcinoma prostatico, sia con finalità adiuvante che radicale. Scansioni di megavoltaggio (MVCT) vengono in genere acquisite giornalmente prima del trattamento per valutare ed eventualmente correggere sia errori di posizionamento che errori legati a possibili movimenti d'organo.*

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*Relativamente a trattamenti adiuvanti, lo studio riporta l'esperienza relativa all'implementazione di strategie di correzione di errori di posizionamento sia di tipo on-line che off-line, in modo da definire la strategia off-line ottimale in grado di ridurre l'errore sistematico di posizionamento. A tal proposito sono analizzati e riportati i dati di 36 pazienti. Relativamente a trattamenti prostatici con finalità radicali sono analizzati e presentati i dati di 21 pazienti, per i quali viene eseguito, uniformemente alla pratica clinica, una correzione giornaliera basata sull'identificazione e la registrazione della prostata, in modo da prendere in considerazione sia errori di posizionamento che possibili movimenti d'organo. Contemporaneamente alla valutazione della componente relativa al movimento d'organo, è stata anche indagata la variabilità inter-osservatori nell'identificazione e visualizzazione della prostata in immagini MVCT. Complessivamente, l'acquisizione di immagini MVCT durante la prima settimana di trattamento con relativa correzione (livello di azione di 3 mm) si mostra un metodo efficace nel ridurre significativamente l'errore sistematico di posizionamento per trattamenti prostatici con finalità adiuvante; la stima dell'errore residuo valutata applicando una strategia di correzione di tipo on-line suggerisce che l'applicazione di un protocollo off-line con correzione dell'errore sistematico di posizionamento dopo la quarta sessione di terapia (senza livello di azione) è in grado di ridurre l'errore sistematico residuo al di sotto di 1,5 mm (1 SD). Un eventuale miglioramento aggiuntivo previsto da un protocollo di correzione di tipo on-line non sembra avere dei vantaggi clinicamente significativi rispetto ad una strategia di tipo off-line; quindi, la possibilità di introdurre nella pratica clinica con tomoterapia elicoidale strategie di tipo off-line potrebbe realmente permettere un risparmio di tempo e risorse. Nel caso di trattamenti radicali, una prima indagine sull'inaccuratezza di registrazione della "prostata" su immagini MVCT mostra una modesta intervariabilità di registrazione, probabilmente a causa del relativamente piccolo impatto del movimento d'organo, dipendente dalle procedure di svuotamento del retto applicate nella pratica clinica. Lo stesso risultato è confermato dalla piccola e non significativa differenza stimata tra la registrazione della posizione della prostata pianificata ed effettiva durante il trattamento sia grazie ad un matching automatico eseguito sulle strutture ossee, che grazie ad una registrazione manuale del medico basata sulla diretta visualizzazione della prostata.*

***PAROLE CHIAVE:*** *Tomoterapia elicoidale, Carcinoma prostatico, Set-up e modellazione nel movimento d'organo.*

## ☐ INTRODUCTION

Helical Tomotherapy Unit (HT) provides an innovative image-guided IMRT technique[9]. Megavoltage CT (MVCT) images of the patient can be generated with the same radiation source used for treatment and can be acquired just before each session to correct patient/tumour positioning. From January 2004 in our Institute around 200 patients were treated for prostate cancer with HT. Image-guidance with MVCT was always used to minimize the impact of set-up and organ motion. However a daily use of MVCT for all patients reduces the number of treatments in a day, because of the additional workload due to MVCT acquisition, matching, evaluation and correction. Main aim of current work is to verify if, under opportunely controlled clinical conditions, the number of MVCTs per patient can be reduced without any significant clinical detriment compared to daily correction.
First, on- and off-line set-up correction strategies[5,6,7,8] were designed on a sample of patient treated with adjuvant intent in order to modelling and to assess the optimal off-line strategies to reduce set-up errors. Second, the results of the analysis of daily MVCT-based correction of prostate position of radical treatments were reported in order to investigate both the set-up and the organ motion component.

## ☐ MATERIAL AND METHODS

### ❐ MVCT Acquisition

On the HT system a conventional 6 MV Linac and a detector array system are mounted opposite each other on a ring gantry that continuously rotates during both the imaging acquisition and the treatment irradiation while the couch continuously translates trough the gantry. The beam is collimated to a fan beam geometry and the imaging geometry is similar to a single-slice helical CT arrangements. For the MVCT imaging, the same radiation source is used with a nominal energy of the electron beam reduced to a lower energy of 3.5 MeV. Three clinical MVCT acquisition modalities (fine, normal, course) are available with corresponding different pitch setting of 1, 2 and 3. All patients were imaged in the normal mode, that means that during one gantry rotation the couch translates for 2 mm; two slices are reconstructed in one rotation. Daily MVCT scans can be registered with planning kVCT images and positioning adjustments may be assessed in order to correct daily set-up and/or organ motion errors. Registration is based on a rigid-body approach (three translational an three rotational degrees of freedom) and may be performed manually or automatically. Previous phantom measu-

rements confirmed that in the clinical condition of pelvic treatment an uncertainty < 1 mm is expected between true and measured shifts when automatic bone matching is applied[10].

### ❒ Prostate Adjuvant treatments: set-up errors modelling

On- and off-line strategies were concomitantly designed to minimize set-up error in patients treated with adjuvant intent; for these patients organ motion was not taken into account, due to the unclear impact of different rectal and bladder filling on the prostatic bed[3]. In any case, as for radical treatments, patients were instructed to carefully empty their rectum and to keep a full bladder at the planning CT scan and before each treatment session. Thirty-seven patients treated with HT with a hypofractionation schedule for prostate adjuvant radiotherapy were selected, 27 of them followed an on-line correction strategy while the remaining patients followed an off-line one. Patients were randomly assigned to one of the two correction strategies and the pilot study on off-line strategy was intentionally closed after a sample of 9 patients.
A median planning target volume (PTV) dose of 58 Gy was prescribed, delivered in 20 fractions (2.9 Gy/fraction). The same margins used in 3DCRT were applied for PTV definition: 8 mm in lateral and in anterior-posterior and 10 mm in cranio-caudal direction[1]. For patient alignment, MVCT images were automatically registered with the planning kVCT images by using the bone matching automatic registration technique; only translational corrections were applied.
■ ***Off-line protocol.*** Concerning the off-line procedure, based on a number of experiences in the use of EPIDs for reducing the systematic set-up error[2,4], MVCT scans were acquired for the first 4 sessions and, after the automatic bone matching, set-up corrections were applied only if one of the estimated shifts was greater than 6 mm; otherwise no corrections were applied during the first 4 sessions. Systematic and random set-up errors were estimated as mean and standard deviation of the shifts reported for the first 4 fractions: a definitive set-up correction of systematic error was then applied at day 5 if it was found to be greater than 3 mm in, at least, one direction. Set-up was then monitored with a weekly MVCT, by re-acquiring the scan prior to treatment and re-matching bone structures: if the estimated shifts were greater than 3 mm a set-up correction was re-applied, otherwise no shifts were implemented. Analysing weekly MVCTs, systematic and random set-up errors were evaluated as standard deviation of the mean shift values and as mean values of standard deviation respectively.
■ ***On-line protocol.*** Concerning the on-line protocol, MVCT scans were consecutively acquired for all 20 sessions and MVCT images were automatically registered on bone structures with reference kVCT images, taking only translations into account. For each session, patient set-up was corrected without considering any actions level. For each session, lateral (x), cranio-caudal (y) and vertical (z) shifts were reported and analyzed. For each patient and for each direction (lateral, cranio-caudal and vertical) set-up residual error was calculated as the difference between the average position during the first fractions and the average position in the remaining part: the set-up residual error at k session is then estimated as the difference between the mean kVCT-MVCT shifts estimated in the first k fraction (mean position) and the reported shift in remaining (n-k) fractions where n is the total number of fractions (in our case n = 20). The population residual systematic error was then assessed as the standard deviation of the mean residual error of the patient population.

### ❒ Prostate radical treatments: set-up and organ motion modelling

Forty five patients treated with HT with a moderately hypofractionation schedule for radical prostate radiotherapy were selected, in which prostate received 71.4-74.2 Gy in 28 fractions. The data of 21 patients who completed the treatment and treated only to prostate and seminal vesicles were analyzed. For all patients, daily MVCT was performed to correct prostate position before treatment. Patients were instructed to carefully emptying the rectum before kVCT and at each fraction. For PTVs definition, the same margins used in our Institution for 3DCRT were applied (LR: 0.8 cm; PA: 0.8 cm; CC: 1 cm).
■ ***Set-up and organ motion modelling.*** MVCT scans were consecutively acquired for all 28 sessions. The position of prostate at each fraction was assessed first through an automatic bone matching with the planning kVCT, by assessing set-up correction and then by adjustment of the physician through direct visualization of the position of prostate to take organ motion component into account. Deviations between

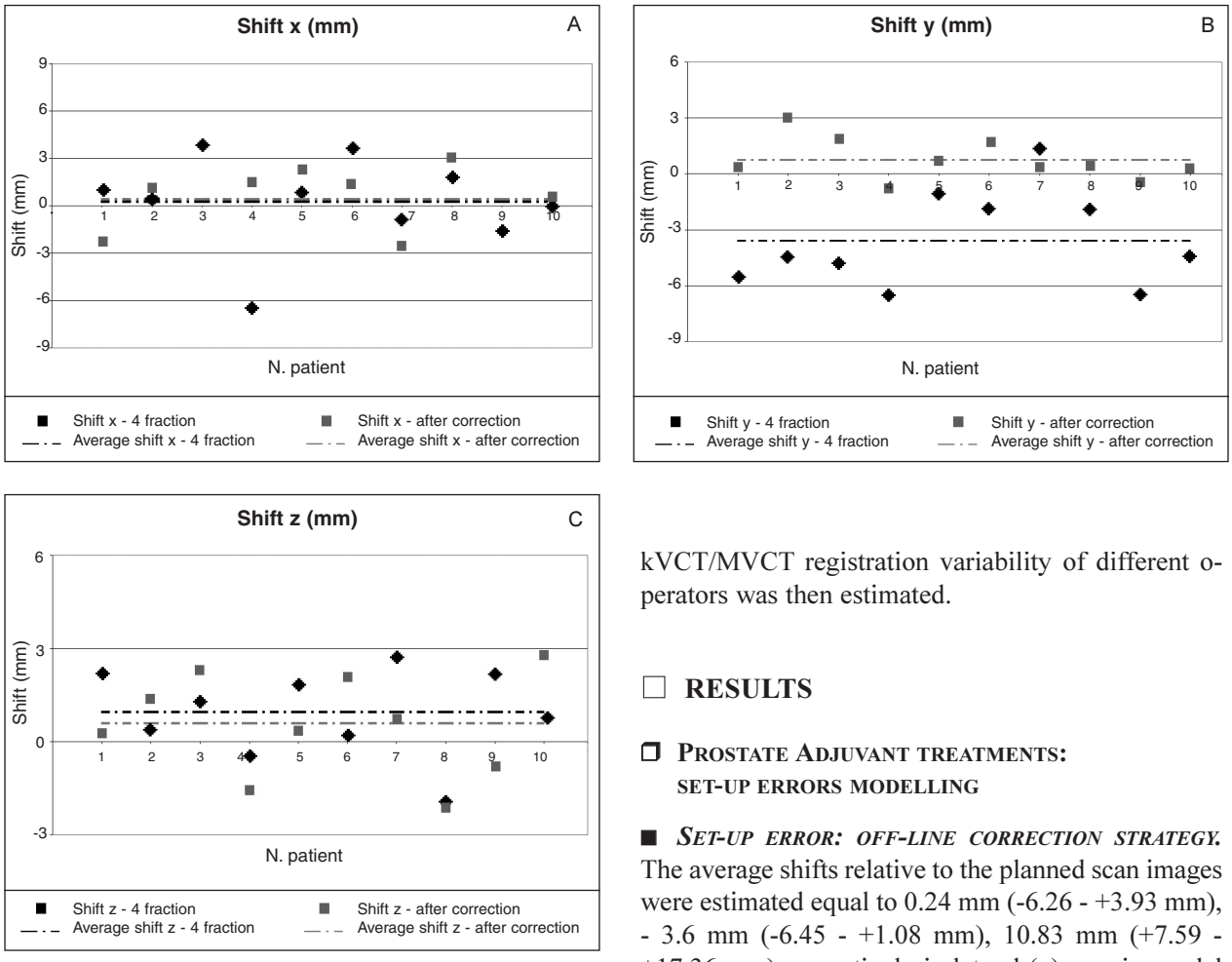


**Figure 1.** Estimated shifts for each patient and for each direction, lateral: x (A), longitudinal: y (B) and vertical: z (C) for the first 4 sessions and for weekly correction.

planning and therapy position assessed by bone match (BM) and by the physician (PM) were registered for the three main axes and for each fraction. Systematic and random components for each patient were assessed; then mean deviation, systematic ($SD_{syst}$) and random ($SD_{random}$) errors were calculated for the whole population. The differences between bone match and physician were also calculated and analysed. Before assessing the organ motion component, an investigation about the uncertainty in tracking the prostate through direct MVCT visualization was started[5,6,11]. Ten MVCT scans of 5 patients (2 MVCT scan per patient) were selected and manually registered with the reference kVCT by 6 physicians by considering first an automatic bone matching and then a visually prostate contour matching adjustment, as routinely done in our clinical practice.

kVCT/MVCT registration variability of different operators was then estimated.

## □ RESULTS

### ❒ Prostate Adjuvant treatments: set-up errors modelling

■ ***Set-up error: off-line correction strategy.*** The average shifts relative to the planned scan images were estimated equal to 0.24 mm (-6.26 - +3.93 mm), - 3.6 mm (-6.45 - +1.08 mm), 10.83 mm (+7.59 - +17.36 mm) respectively in lateral (x), cranio-caudal (y) and vertical (z) directions. The vertical disagreement, due to a sag of the couch during the longitudinal movement, is then reduced to an average shift of 0.92 mm (-1.88 - +2.83 mm), by considering the difference of patient's position relative to the first fraction.

The systematic residual error, estimated by the post-correction weekly MVCT, was within 3 mm: mean deviation equal to 0.36 mm (-2.70 - +3.03 mm), 0.74 mm (-0.75 - +2.98 mm) and 0.57 (-1.95 - +2.86 mm) were estimated respectively in lateral, cranio-caudal and vertical directions. The number of corrections > 3 mm for weekly MVCT was 10, 4 and 5 respectively for lateral, longitudinal and vertical direction respectively. The lateral position was the most crucial direction; the reason was probably related to difficulties for the radiographer in patient positioning because there is no an automatic adjustment of couch in this direction and the light field in not perfectly visible on the patient skin. Figure 1 shows the estimated shifts for the nine patients considering both the first 4 ses-

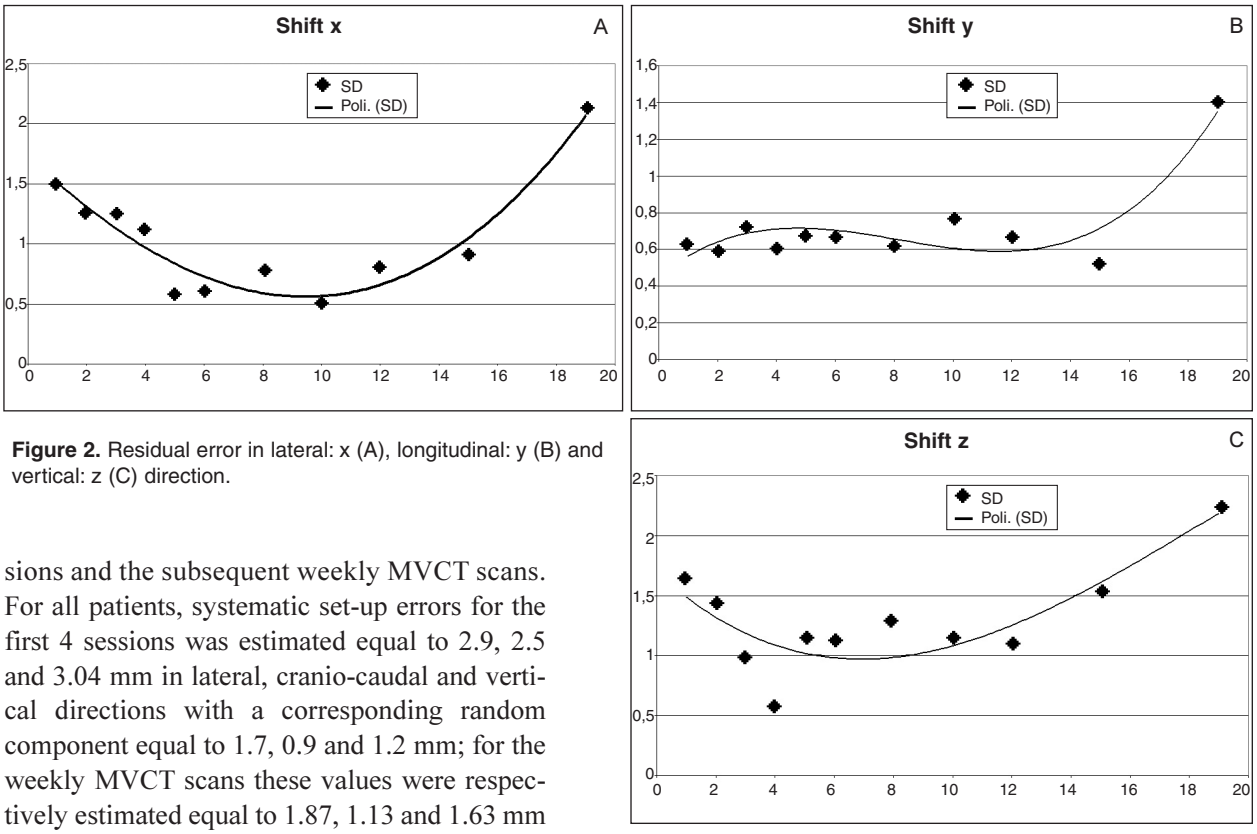


**Figure 2.** Residual error in lateral: x (A), longitudinal: y (B) and vertical: z (C) direction.

sions and the subsequent weekly MVCT scans. For all patients, systematic set-up errors for the first 4 sessions was estimated equal to 2.9, 2.5 and 3.04 mm in lateral, cranio-caudal and vertical directions with a corresponding random component equal to 1.7, 0.9 and 1.2 mm; for the weekly MVCT scans these values were respectively estimated equal to 1.87, 1.13 and 1.63 mm for the systematic component and 2.42, 1.51 and 1.63 mm for the random one.

■ ***SET-UP ERROR: ON-LINE CORRECTION STRATEGY.*** The results found with the on-line strategy were consistent with the off-line correction analysis. Based on the on-line procedure, systematic and random components of the whole population were both < 3 mm (1SD): estimated systematic errors were equal to 2.78 mm, 2.32 mm and 2.43 mm for lateral, longitudinal and vertical directions and respectively equal to 2.68 mm, 1.29 mm and 1.89 mm for the random component. A systematic residual error < 2 mm for all direction was in general found when assessing the systematic error at the third or fourth session. A systematic residual error < 1.5 mm was estimated at first session for 16 patients in lateral direction, 25 patients for the cranio-caudal and in 18 patients for the vertical direction. Figure 2 shows the residual error as a function of the session number. The initial reduction of the residual error was caused by the improved estimate of the average patient set-up with the increased number of measurements. The minimum residual error was achieved in correspondence of the $7^{th}$-$10^{th}$ session; however, just after 3-4 MVCT scans the residual systematic error was reduced to less than 1.5 mm for all three directions; in other words the benefit in reducing the residual systematic error after the first 3-4 sessions seems not to be clinically significant. After reaching a minimum value the residual error increased because the estimate of the patient set-up during the remaining part of the treatment becomes more uncertain due to the limited number of repeated MVCT scans.

A number of investigations reported a significant reduction of systematic error after collecting a sample of set-up images during the first week of the treatment. In particular, it was shown that for a significant fraction of patients the correction of set-up error based only on the first fraction is not enough in detecting potentially detrimental set-up errors. Our results confirm these findings, showing that less than two third of the patients can reduce the systematic error below 1.5 mm (1 SD) with only one set-up correction at the first fraction.

### ❒ PROSTATE RADICAL TREATMENTS: SET-UP ERRORS AND ORGAN MOTION MODELLING

Data of 522 fractions were available. Mean bone

match deviations for the three main axes were -1.4, -2.2 and -0.5 mm respectively for lateral, longitudinal and vertical axes with $SD_{syst}$ of 1.6, 1.3 and 3.4 mm and $SD_{random}$ of 3.4, 1.9 and 2.3 mm respectively for lateral, cranio-caudal and vertical directions. The deviation between bone match and physician registration was very small with mean deviation below 0.1 mm, $SD_{syst}$ around 0.3 mm and $SD_{random}$ up to 0.9 mm for the vertical direction. Looking at this axis (PA), only 4/522 (0.6%) and 15/522 (2.9%) fractions showed a deviation between PM and BM ≥ 5 mm and 3 mm respectively. The inter-observer variability for direct prostate visualization and match was also found to be very small, with a maximum value for vertical shift around 0.8 mm (1 SD).
The final registration performed by the physicians compares well with the automatic bone registration for the considered ten MVCT scans; as a consequence, a small inter-observer variation was found. These preliminary results indirectly suggest a prevalence of set-up error over organ motion uncertainties probably due to the effectiveness of rectum emptying procedures routinely applied before planning CT and before each treatment session.

## CONCLUSIONS

MVCT-based daily correction was a feasible and efficient procedure. Using MVCT during the first week of the treatment with an action level equal to 3 mm, was found to be effective in significantly reducing systematic set-up error for adjuvant prostate treatment; the estimate of the residual error from the on-line correction strategy analysis suggests that the application of an off-line protocol with systematic set-up correction after the first 4 session without any action level may further reduce the residual systematic error below or around 1.5 mm (1 SD). Compared to such off-line approach, the additional improvement of on-line correction does not seem to be clinically relevant.
Concerning prostate registration, a small inter-user variability of prostate image registration was found. Daily MVCT on a group of patients treated for radical prostate whose rectum is carefully emptied before treatment seems to show a lower impact of organ motion compared to other investigations. The possibility to implement in our clinical practice off-line approaches also for radical treatments should be more investigated, but preliminary results seems to show this potential.

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