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Evaluation of a dedicated software for semi-automated VMAT planning of spine Stereotactic Body Radiotherapy (SBRT)

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Abstract

Purpose

To determine whether SBRT of spinal metastasis using a dedicated treatment planning system (TPS) and delivered with a gantry-based LINAC could provide plans of similar quality to the Cyberknife technology. Additional comparison was also done with other commercial TPS used for volumetric modulated arc therapy (VMAT) planning.

Materials and Methods

Thirty Spine SBRT patients, previously treated in our institution with CyberKnife (Accuray, Sunnyvale) using Multiplan TPS, were replanned in VMAT with an dedicated TPS (Elements Spine SRS, Brainlab, Munich) and our clinical TPS (Monaco, Elekta LTD, Stockholm), using exactly the same arc geometry. The comparison was done by assessing differences in dose delivered to PTV, CTV and spinal cord, calculating modulation complexity scores (MCS) and performing quality control (QA) of the plans.

Results

Regardless of the vertebra level, in general, no statistical difference was found in PTV coverage between all TPS. Conversely, PTV and CTV $D_{50\%}$ were found significantly higher for the dedicated TPS compared to others. In addition, the dedicated TPS also resulted in better gradient index (GI) than clinical VMAT TPS, whatever the vertebral level, and better GI than Cyberknife TPS for the thoracic level only. The $D_{2\%}$ to the spinal cord was generally significantly lower with the dedicated TPS compared with others. No significant difference was found in the MCS between both VMAT TPS. All QA were clinically acceptable.

Conclusion

The Elements Spine SRS TPS offers very effective and user-friendly semi-automated planning tools and is secure and promising for gantry-based LINAC spinal SBRT.

1. Introduction

For oligometastatic patients, spine stereotactic body radiation therapy (SBRT) is an extending alternative to the classical palliative fractionation regimen [1]. The improvements in systemic therapy lines allow a benefit in patient survival, and SBRT can lead to a durable local control with very limited neurologic side effects [2], [3]. Spine SBRT planning is challenging because of the close vicinity between the spinal cord, having strict dose constraints, and the Planning Target Volume (PTV). Consequently, a high dose gradient is required to achieve the dosimetric objectives. For this reason, spine SBRT has historically been preferentially delivered using robotic radiosurgery. The CyberKnife (Accuray, Sunnyvale) provides steep dose gradients by using multiple non-coplanar beams, and can therefore be considered as the “gold standard” technology.

In parallel, new perspectives of treatments have emerged with last generation gantry-based linear accelerators (LINAC) equipped with highly performing imaging devices, thus enabling an increased accuracy in dose delivery. Therefore, dose planning and delivery of spine SBRT is now commonly performed with versatile treatment planning systems (TPS) using volumetric modulated arc therapy (VMAT) technique [4], [5].

Simultaneously, specialized planning solutions are also elaborated. The Elements TPS (Brainlab, Munich) has been developed according to this philosophy, with specific modules dedicated to stereotactic radiosurgery (SRS): Cranial SRS, Multiple Brain Mets SRS or Spine SRS [6], [7]. Elements Spine SRS (E-SRS) allows an automated VMAT planning process, based on the use of templates defining beam geometry and dosimetric objectives on organs at risk (OAR) and target volumes. The optimization algorithm in E-SRS has been specifically designed to facilitate high dose gradient at the spinal cord to PTV interface. This is particularly important for targets with complex and concave shapes, e.g. when the whole vertebrae has to be treated. The optimization algorithm includes an arc duplication option enabling PTV splitting into several low complexity elementary volumes treated separately with one or several arc each. Such a decomposition should also result in treatment plans with the same or higher quality than non-dedicated TPS [6]. Another advantage of E-SRS is that the planning process is semi-automated. Hence, it should allow less inter-operator variability than conventional TPS while saving planning time.

The dosimetric performances of E-SRS TPS compared with other clinical TPS were evaluated in 4 different studies [6], [7], [8], [9]. In two recent studies, the dosimetric superiority of Elements Spine SRS compared with Eclipse TPS (Varian Medical Systems, Palo Alto, USA), in terms of spinal cord sparing [6], [7] and gradient index [9] was observed. In another study comparing the same TPS, *Piliero et al.* [8] concluded to a similar plan quality between both TPS. E-SRS was also compared to Monaco (Elekta LTD, Stockholm) and Pinnacle (Phillips, The Netherlands), showing a dosimetric superiority of E-SRS plans with a better ability to satisfy all the constraints simultaneously [9]. Finally, the feasibility of the clinical application of the TPS was demonstrated through the evaluation of the local control in 32 patients, with an 86% local control rate at 6 and 9 months [10].

In this study, we evaluated for the first time the performances of E-SRS 3.0 TPS with comparison to plans generated with the SRS dedicated Cyberknife TPS (Multiplan 5.1.2 Accuray, Sunnyvale, USA) on a large cohort of 35 patients previously treated in our institution with the CyberKnife. Similar to other work, a comparison with the TPS that we use routinely for our standard VMAT treatments (Monaco V5.51, Elekta, Crawley, UK) was also done on the same patients' cohort [9]. The objective was to investigate the real gain brought by the TPS, free from the technical benefit potentially linked to the treatment machine. The comparison of the different solutions was based on dosimetric and geometric indices. The complexity of

VMAT plans provided by Monaco and E-SRS was finally assessed by calculating modulation complexity scores (MCS) [11] and analysing EPID-based quality assurance (QA) results.

2. Materials and methods

2.1. Patients and clinical protocol

Thirty-five patients previously treated with the CyberKnife for spine metastasis were included in this study which was approved by the hospital ethics committee. Targets and OARs were contoured according to the international guidelines [12]. The PTVs were generated by adding a 2 mm margin to the clinical target volumes (CTVs). A 2 mm margin around the OARs was added to define planning organ at risk volumes (PRV). According to UK SABR consortium [13], optimization volumes, excluding spinal cord PRV, were also generated to facilitate the optimization. In this study, the PTV coverage evaluation was performed on this PTV excluding spinal cord. The patient sample was sorted according to the vertebral level as follows: cervical (n = 10 patients), thoracic (n = 15 patients) and lumbar (n = 10 patients). The prescribed dose was 30 or 35 Gy delivered in 5 fractions to the PTV. A description of the patient cohort is provided in Table 1. The average volume of the PTVs was $38.3 \pm 25.5 \text{ cm}^3$. The affected spinal regions were very different from one patient to the other, leading to target volumes of varying complexity.

Table 1. Cohort description.

Number of patients	35
Sex ratio (F/M)	23/12
Median age (interval)	65 (38–89)
Vertebral Level	
Cervical	10 (28.57%)
Thoracic	15 (42.85%)
Lumbar	10 (28.57%)
PTV volume (cc) mean \pm standard deviation (interval)	
Cervical	16.17 \pm 7.39 (6.64–32.35)
Thoracic	39.52 \pm 25.06 (13.08–99.43)
Lumbar	58.65 \pm 20.6 (43.06–100.98)
Dose de prescription	
30 Gy in 5 fractions	23 (65.71%)
35 Gy in 5 fractions	12 (34.29%)

2.2. Treatment planning

Clinical plans were performed on MultiPlan TPS and delivered with a CyberKnife VSI robotic surgery system. Up to 3 cones from 10 mm to 50 mm diameter were used to deliver 6FFF MV multiple non-coplanar photon beams. The Monitor Units (MU) and number of nodes

were optimized to limit the treatment duration from 35 to 45 min per fraction. Typically, total MU were limited to 11,000 to achieve this objective. Due to the robot geometrical limitation of this CyberKnife version, posterior beams were limited to an angle of 15° from the couch top, leading to a very limited number of posterior incidences. The final dose distribution was calculated in sequential mode using the Ray Tracing (RT) algorithm.

Each case was blindly replanned in VMAT using E-SRS 3.0 TPS. Two coplanar 360° arcs were used with collimator angle set to 80° during clockwise (CW) rotation and 280° during counterclockwise (CCW) rotation. Duplication was enabled to allow up to 4 arcs to be used to deliver the treatment, with a maximum of 90 control points (CP) per arc. The final dose distribution was calculated to medium with MC algorithm using a 2% variance and a 2 mm grid size.

VMAT plans were finally performed with Monaco 5.51 TPS using 2 CW/CCW 360° arcs, leading to 4 arcs. The collimator angles were set to 80° and 280° for each CW/CCW arc, respectively. A minimum segment width of 0.5 cm, a medium smoothing filter and a maximum of 150 CP per arc, were used, respectively, as segmentation parameters. The final dose distribution was calculated to medium with MC algorithm using a 1% variance and a 2 mm grid size.

Monaco and E-SRS treatment plans were delivered using 6 MV photon beams from a VersaHD (Elekta AB, Stockholm, Sweden) equipped with an Agility collimator with 5 mm leaves at isocenter.

2.3. Dosimetric goals

Similarly to the CyberKnife treatment plans, a dose of 30 or 35 Gy in 5 fractions was prescribed at the 80% isodose. Hence the objectives for VMAT replanning with both TPS were to respect a maximal dose that mimics a prescription on the 80% isodose. The planning objective was consistent with the UK SABR consortium guidelines for spinal metastases [13], which recommends a minimum PTV coverage with the prescription isodose of 95%. This objective was not mandatory in case of epiduritis. Hot spot of 125% of the prescribed dose was tolerated within the PTV. The dose constraints published by R. Timmerman for a 5-fractions treatment were used to set the dose constraints to the OARs, in accordance with our institution's clinical practices [14]. Hence the main constraints were to respect a maximum dose of ≤ 30 Gy, ≤ 34 Gy, ≤ 35 Gy and ≤ 38 Gy to the PRVspinal cord, PRV spinal canal, PRVesophagus and PRVtrachea, respectively, and a dose received by 200 cm³ of kidney ≤ 17.5 Gy.

2.4. Dosimetric analysis

Dose distributions and Dose Volume Histograms (DVH) were analyzed in an independent software, MIM Maestro 7.0.2 (MIM software Inc., Cleveland, USA), using a dedicated workflow. All plans were resampled in MIM to a 2 mm grid size.

The different plans were compared by assessing differences in PTV $V_{100\%}$, $D_{2\%}$, $D_{50\%}$ and $D_{98\%}$, and $D_{2\%}$, CTV $D_{50\%}$, and D_{max} to the PRVspinal cord. Dose conformation was characterized with Paddick Conformity Index (PCI):

$$PCI = \frac{TV_{PTV}^2}{TV \times PIV}$$

where TV_{PTV} is the PTV volume covered by prescription isodose, TV is the PTV volume, and PIV is the volume of prescription isodose.

Dose fall-off was evaluated using Gradient Index (GI):

$$GI = \frac{PIV_{50}}{PIV}$$

where PIV_{50} is the volume of half the prescription isodose and PIV is the prescription isodose.

In addition, plan quality indexes (PQI) were calculated, derived from the formula proposed by *Jornet et al. [15]*, to compare planning goals achievement among TPS. Sub-PQI focusing on target metrics (PQI_{target}), on PRVspinal cord constraints (PQI_{OAR}) and on the dose conformation ($PQI_{indices}$) were first calculated according to the following formulas:

$$\begin{aligned} PQI_{target} = & w \\ & \times \frac{V_{100\%,plan}(PTV) - V_{100\%,goal}(PTV)}{V_{100\%,goal}(PTV)} + \frac{D_{98\%,plan}(PTV) - D_{98\%,goal}(PTV)}{D_{98\%,goal}(PTV)} \\ & + \frac{D_{2\%,goal}(PTV) - D_{2\%,plan}(PTV)}{D_{2\%,goal}(PTV)} + \frac{D_{50\%,goal}(CTV) - D_{50\%,plan}(CTV)}{D_{50\%,goal}(CTV)} \end{aligned}$$

where a value of 2 was attributed to w to give a higher importance to PTV coverage during the clinical validation of treatment plans.

$$PQI_{OAR} = \frac{D_{max,goal}(PRVspinalcord) - D_{max,plan}(PRVspinalcord)}{D_{max,goal}(PRVspinalcanal)}$$

$$PQI_{indices} = \frac{PCI_{plan} - PCI_{goal}}{PCI_{goal}} + \frac{GI_{goal} - GI_{plan}}{GI_{goal}}$$

For all three PQIs, goal values are reported in [Table 2](#), and were chosen based on our clinical constraints and experience for PTV $V_{100\%}$, spinal cord D_{max} , pCI and GI. They were derived from average values over all Cyberknife plans for each prescription scheme for PTV $D_{98\%}$, PTV $D_{2\%}$ and CTV $D_{50\%}$ assuming that Cyberknife was our gold standard in this study. Finally, a global PQI was obtained by using the following formula:

$$PQI_{global} = PQI_{target} + PQI_{OAR} + PQI_{indices}$$

Table 2. Goals list and weighting factor for the metrics involved in PQI calculations.

Structures/Indices	Goal	PQI weighting
PTV	$V_{100\%} \geq 95\%$ PTV $D_{98\%} \geq \text{Mean Cyberknife } D_{98\%}$: $D_{98\%} \geq 29.3$ Gy, for 30 Gy prescription dose $D_{98\%} \geq 33$ Gy, for 35 Gy prescription dose $D_{2\%} \leq \text{Mean Cyberknife } D_{2\%}$: $D_{2\%} \leq 36.6$ Gy, for 30 Gy prescription dose $D_{2\%} \leq 43.75$ Gy, for 35 Gy prescription dose	2
CTV	$D_{50\%} \leq \text{Mean Cyberknife } D_{50\%}$: $D_{50\%} \leq 34.1$ Gy, for 30 Gy prescription dose $D_{50\%} \leq 41.4$ Gy, for 35 Gy prescription dose	
PRVspinal cord	$D_{\max} \leq 30$ Gy	
pCI	$pCi \geq 0.8$	
GI	$GI \leq 4$	

2.5. Modulation complexity score and plan quality assurance

For VMAT plans only, a modulation complexity score (MCS) was calculated from the segments' details report (segment shape, area and weight) extracted from the TPS following the formula introduced by *Mc Niven* et al. [11]. The number of MU and control points were also reported as indicators of modulation complexity.

To verify deliverability of the plans, QA measurements were performed for 10 patients randomly chosen, using electronic portal imaging device (EPID) and ThinkQA EPIbeam 1.0.6.21 software (DOSIsoft, Cachan, France). The passing criteria was local gamma index with 2%-2 mm tolerance with a 10% threshold. The passing rate was expected to be above 95%.

2.6. Statistical analysis

For assessing the statistical significance ($p < 0.05$), all differences between manual and automatically generated plans were evaluated using Wilcoxon signed ranks test.

3. Results

3.1. Dosimetric analysis

An example of dose distributions and dose-volume histograms obtained with the three TPS, for one patient, are presented in Fig. 1, Fig. 2, respectively, and the results for all dosimetric parameters summarized in Table 3, Table 4, Table 5 for cervical, thoracic and lumbar vertebrae, respectively. Regardless of the vertebra level, PTV $V_{100\%}$ and PTV $D_{98\%}$ were not statistically different between all the TPS ($p > 0.107$), except for the thoracic level where Monaco showed better PTV $V_{100\%}$ than Multiplan ($p = 0.026$) (Table 4). Conversely, PTV $D_{50\%}$ of E-SRS treatment plans were found to be significantly higher ($p < 0.004$) in 35 and in 34 out of 35 treatment plans, compared to Multiplan and Monaco, respectively, with PTV $D_{50\%}$ being up to 1.8 Gy higher than with other solutions at the lumbar level. On the contrary,

PTV $D_{50\%}$ were not significantly different between Monaco and Multiplan ($p > 0.063$), with the exception of the thoracic level, where it was significantly superior with Monaco than with Multiplan ($p = 0.015$). CTV $D_{50\%}$ were also significantly higher with E-SRS TPS compared to other TPS ($p < 0.031$), whatever the vertebra level, with $D_{50\%}$ to the CTV being up to 1.6 Gy higher than with other TPS. In contrast, CTV $D_{50\%}$ were not significantly different between Monaco and Multiplan ($p\text{-value} > 0.063$). Consequently, PTV $D_{2\%}$ was found significantly higher with E-SRS than with other TPS ($p < 0.004$) and also significantly different between Monaco and Multiplan ($p < 0.002$) with a PTV $D_{2\%}$ slightly lower in Monaco than in Multiplan, with the exception of the cervical level ($p = 0.131$).

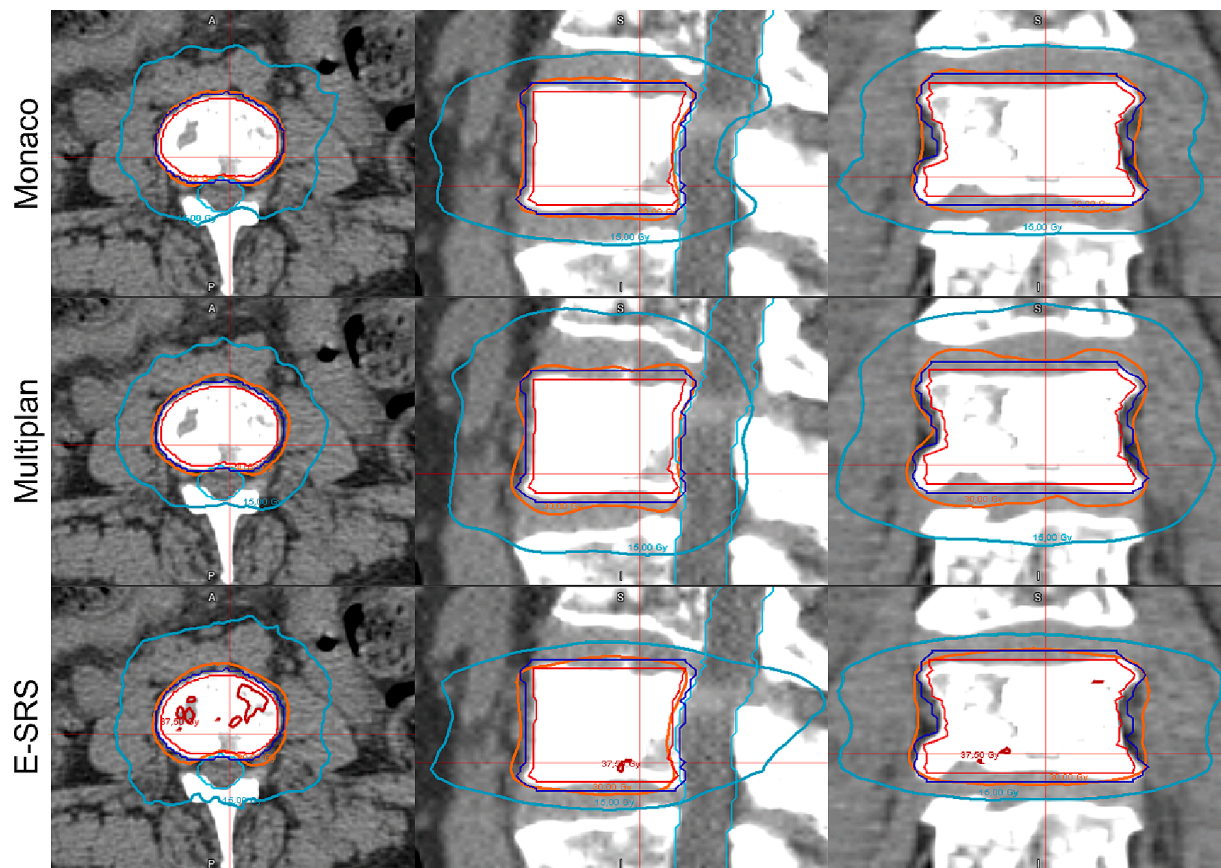


Fig. 1. Axial, sagittal and coronal views of Monaco, Multiplan and Elements Spine SRS dose distributions for one patient. The CTV is in red, the PTV is in blue, and the spinal canal in cyan. 100% isodose line is thick orange line, 50% isodose line is thick cyan line (prescribed dose: 30 Gy in 5 fractions) and 125% isodose line is in thick red. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

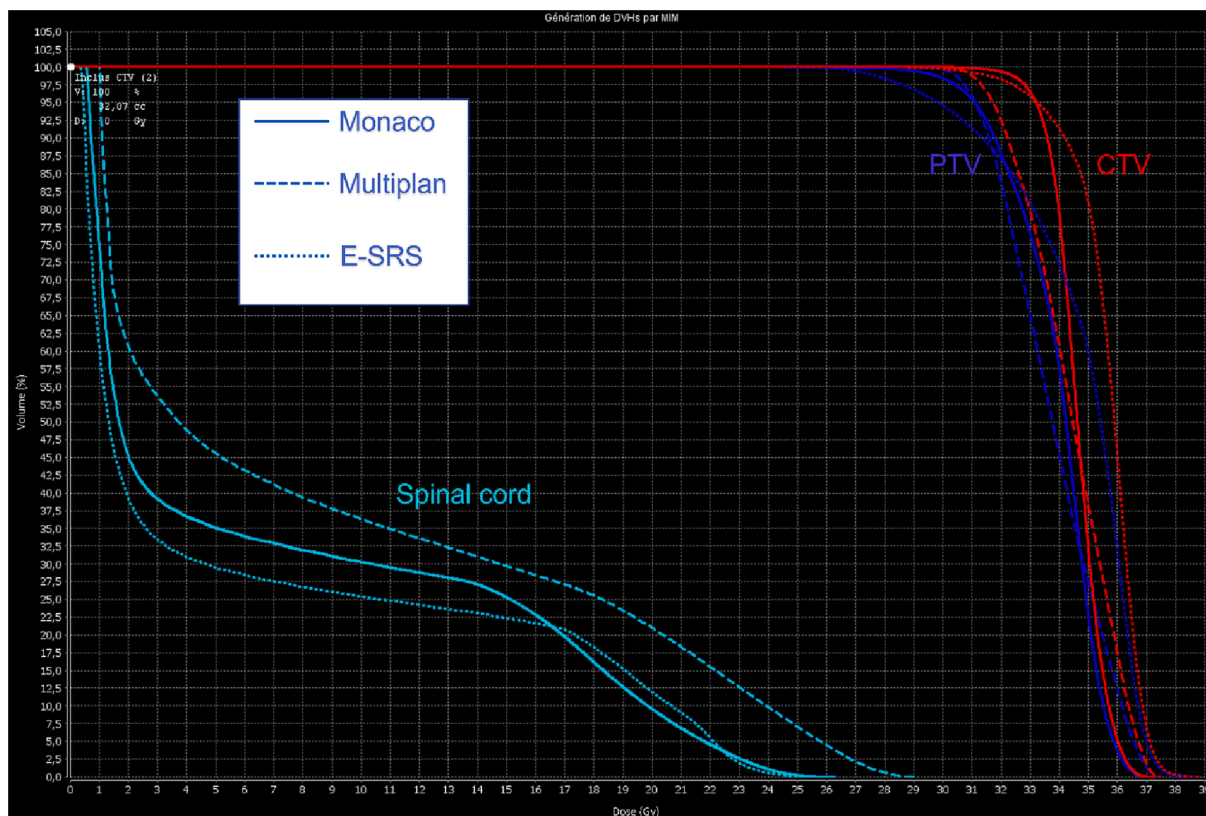


Fig. 2. Dose volume Histograms for the patient presented in Fig. 1.

Table 3. Summary of dosimetric results for cervical vertebrae plans. Values are average across the ten cases.

Cervical Vertebrae Plans		E-SRS Mean [range]	Multiplan Mean [range]	Monaco Mean [range]
PTV $V_{100\%}$ (%)		96.1 [93.0–98.5]	94.5 [85.3–99.6]	96.2 [92.5–98.9]
30 Gy (8 patients)	PTV D2% (Gy)	37.3 [37.2–37.4]	36.6 [36.1–37.4]	36.2 [35.4–37.3]
	PTV D50% (Gy)	35.0 [34.3–35.6]	33.5 [32.4–34.3]	33.8 [33.1–34.3]
	PTV D98% (Gy)	29.4 [28.6–30.3]	28.6 [20.4–30.6]	28.6 [20.1–30.4]
	CTV D50% (Gy)	35.7 [35.1–36.2]	34.1 [32.9–35.6]	34.4 [33.7–35.0]
35 Gy (2 patients)	PTV D2% (Gy)	43.3 [43.3–43.4]	42.9 [42.9–43.0]	42.7 [42.6–42.7]
	PTV D50% (Gy)	39.9 [39.8–40.2]	39.1 [38.6–39.5]	39.5 [38.9–40.0]
	PTV D98% (Gy)	33.6 [33.3–33.9]	32.5 [31.5–33.4]	33.9 [33.6–34.1]
	CTV D50% (Gy)	41.0 [40.9–41.2]	40.2 [40.1–40.2]	40.3 [39.8–40.8]
	CI	0.79 [0.73–0.87]	0.77 [0.68–0.86]	0.77 [0.58–0.84]
	GI	3.95 [3.60–4.29]	3.97 [3.13–5.08]	5.13 [4.07–6.65]
Dose to Spinal Cord PRV	Dmax (Gy)	29.0 [26.6–31.3]	29.3 [25.9–32.6]	28.9 [25.6–31.8]
	D2% (Gy)	23.9 [20.2–26.9]	26.2 [23.3–28.6]	24.5 [21.3–28.8]

Table 4. Summary of dosimetric results for thoracic vertebrae plans. Values are average across the fifteen cases.

Thoracic Vertebrae Plans		E-SRS Mean [range]	Multiplan Mean [range]	Monaco Mean [range]
PTV V _{100%} (%)		96.1 [92.0–98.8]	95.1 [89.6–98.4]	96.7 [91.0–98.7]
30 Gy (11 Patients)	PTV D2% (Gy)	37.2 [36.3–37.5]	36.6 [36.4–36.8]	36.3 [35.3–36.7]
	PTV D50% (Gy)	35.2 [34.5–35.6]	33.5 [32.8–34.3]	34.0 [33.2–34.5]
	PTV D98% (Gy)	29.4 [28.7–30.6]	29.5 [28.2–30.1]	29.7 [28.7–30.3]
	CTV D50% (Gy)	35.6 [35.0–35.9]	34.2 [33.5–34.9]	34.4 [33.5–35.1]
35 Gy (4 patients)	PTV D2% (Gy)	43.4 [43.3–43.4]	42.8 [42.6–43.1]	42.1 [40.9–42.7]
	PTV D50% (Gy)	40.9 [39.8–41.5]	39.3 [39.1–39.5]	39.5 [38.6–40.2]
	PTV D98% (Gy)	33.1 [32.4–34.6]	33.0 [32.5–33.3]	33.3 [30.2–34.7]
	CTV D50% (Gy)	41.4 [40.6–41.9]	40.1 [39.8–40.4]	40.0 [38.8–40.8]
	CI	0.80 [0.67–0.89]	0.78 [0.69–0.84]	0.78 [0.61–0.88]
	GI	3.75 [2.99–4.43]	4.31 [3.47–5.66]	4.22 [3.45–5.48]
Dose to Spinal Cord PRV	Dmax (Gy)	29.4 [28.7–30.8]	29.9 [28.6–30.6]	29.4 [26.1–30.8]
	D2% (Gy)	25.4 [19.7–27.3]	27.1 [20.0–27.7]	26.4 [21.2–29.8]

Table 5. Summary of dosimetric results for lumbar vertebrae plans. Values are average across the ten cases.

Lumbar Vertebrae Plans		E-SRS Mean [range]	Multiplan Mean [range]	Monaco Mean [range]
PTV V _{100%} (%)		96.0 [94.7–98.4]	96.0 [90.6–99.8]	96.6 [94.8–99.0]
30 Gy (4 patients)	PTV D2% (Gy)	37.34 [37.1–37.5]	36.59 [36.3–36.8]	36.2 [35.6–36.5]
	PTV D50% (Gy)	35.39 [34.8–35.8]	33.91 [33.1–35.2]	33.9 [33.4–34.2]
	PTV D98% (Gy)	29.35 [28.5–30.3]	30.20 [29.6–30.7]	29.8 [28.4–30.4]
	CTV D50% (Gy)	35.59 [35.3–35.9]	34.01 [33.6–34.4]	34.5 [34.5–34.6]
35 Gy (6 patients)	PTV D2% (Gy)	43.54 [43.3–43.8]	42.68 [42.4–42.9]	42.3 [42.0–42.6]
	PTV D50% (Gy)	41.16 [40.5–41.5]	39.38 [38.7–39.8]	39.9 [39.7–40.2]
	PTV D98% (Gy)	33.21 [31.7–34.1]	33.30 [31.8–34.6]	32.8 [31.4–33.4]
	CTV D50% (Gy)	41.61 [40.7–42.1]	39.8 [39.3–40.5]	40.1 [39.3–40.7]
	CI	0.83 [0.77–0.89]	0.79 [0.71–0.84]	0.83 [0.76–0.92]
	GI	3.60 [3.38–3.96]	3.75 [3.26–4.90]	3.97 [3.60–4.51]
Dose to Spinal Cord PRV	Dmax (Gy)	29.1 [27.9–31.6]	29.8 [27.8–31.8]	28.9 [26.3–30.9]
	D2% (Gy)	25.0 [22.8–26.6]	26.6 [22.6–29.3]	25.7 [22.9–28.4]

Regarding the PCI, no significant difference was observed between the 3 vertebrae levels. On average, at equivalent PTV coverage, higher PCI indices were obtained at the lumbar level for all the TPS. The PCI were not statistically different for all vertebral levels, with the exception of the lumbar level, where E-SRS plans resulted in better PCI compared to Monaco ($p = 0.032$) and Multiplan ($p = 0.024$).

E-SRS plans also resulted in better GI than Monaco plans, whatever the vertebral level ($p < 0.009$), and better GI than Multiplan plans for the thoracic level only ($p = 0.007$) (Table 4). Finally, the GI was significantly better in Multiplan than in Monaco for the cervical level only ($p = 0.006$), whereas no statistical difference was observed on other vertebral levels ($p \geq 0.232$).

The D_{max} to the spinal cord was respecting the dose constraints criteria for all the treatment plans (Table 3, Table 4, Table 5), and no significant difference was found between the TPS, except between Multiplan and E-SRS on the thoracic level ($p = 0.008$). In contrast, the $D_{2\%}$ to the spinal cord was found to be significantly lower with E-SRS compared to Multiplan in 30 out of 35 treatment plans ($p < 0.037$), and compared to Monaco at the thoracic level only, for 11/15 instances ($p = 0.038$). Regarding Monaco and Multiplan TPS, $D_{2\%}$ to the spinal cord was significantly lower for Monaco compared to Multiplan for the cervical level ($p = 0.037$), while there was no significant difference observed for other vertebrae levels ($p > 0.188$).

Regarding the number of MU, on average, Multiplan plans had up to 4.5 times and 3 times more MU than E-SRS and Monaco plans, respectively (Table 6).

Table 6. Summary of average total MU for the three TPS, per vertebral level and for all patients.

Empty Cell	E-SRS Total MU: Mean [range]	Multiplan Total MU: Mean [range]	Monaco Total MU: Mean [range]
Cervical plans	7476 [5730–12385]	30,850 [18242–43251]	10,365 [7189–15050]
Thoracic plans	9233 [6950–12880]	41,546 [16303–76623]	14,614 [9939–22092]
Lumbar plans	9845 [7620–18700]	46,998 [35376–56432]	16,495 [10246–21705]
All plans	8906	40,048	13,938

Finally, the PQIglobal scoring did not reflect a significant superiority of Cyberknife plans over E-SRS and Monaco plans, with a better scoring obtained on 13 patients versus 12 and 10 patients for E-SRS and Monaco, respectively (Fig. 3).

Furthermore, for several patients (i.e. P5, P10, P12, P13 and P33), the PQIglobal of Cyberknife plans were significantly lower than for VMAT plans. The same observation was done for some Monaco plans (i.e. P8, P11, P27) in comparison with the two other techniques. Note that for P24, Cyberknife and Monaco plans had a significantly lower score than E-SRS plans. Finally, E-SRS plans presented the narrowest dispersion of points over all the patients' cohort.

PQItarget scoring reflected the superiority of Monaco plans compared with E-SRS and Cyberknife, with 22 patients over 35 having better scoring than the two other modalities. In contrast, the PQIindices calculation showed the superiority of the 2 other techniques compared with Monaco, each of the 2 techniques having obtained the best score for 11 patients. Finally, PQIoar scoring showed the superiority of E-SRS and Monaco plans over Cyberknife plans, with a better scoring obtained on 16 and 15 patients for E-SRS and Monaco, respectively, versus 4 for Cyberknife plans (Fig. 3).

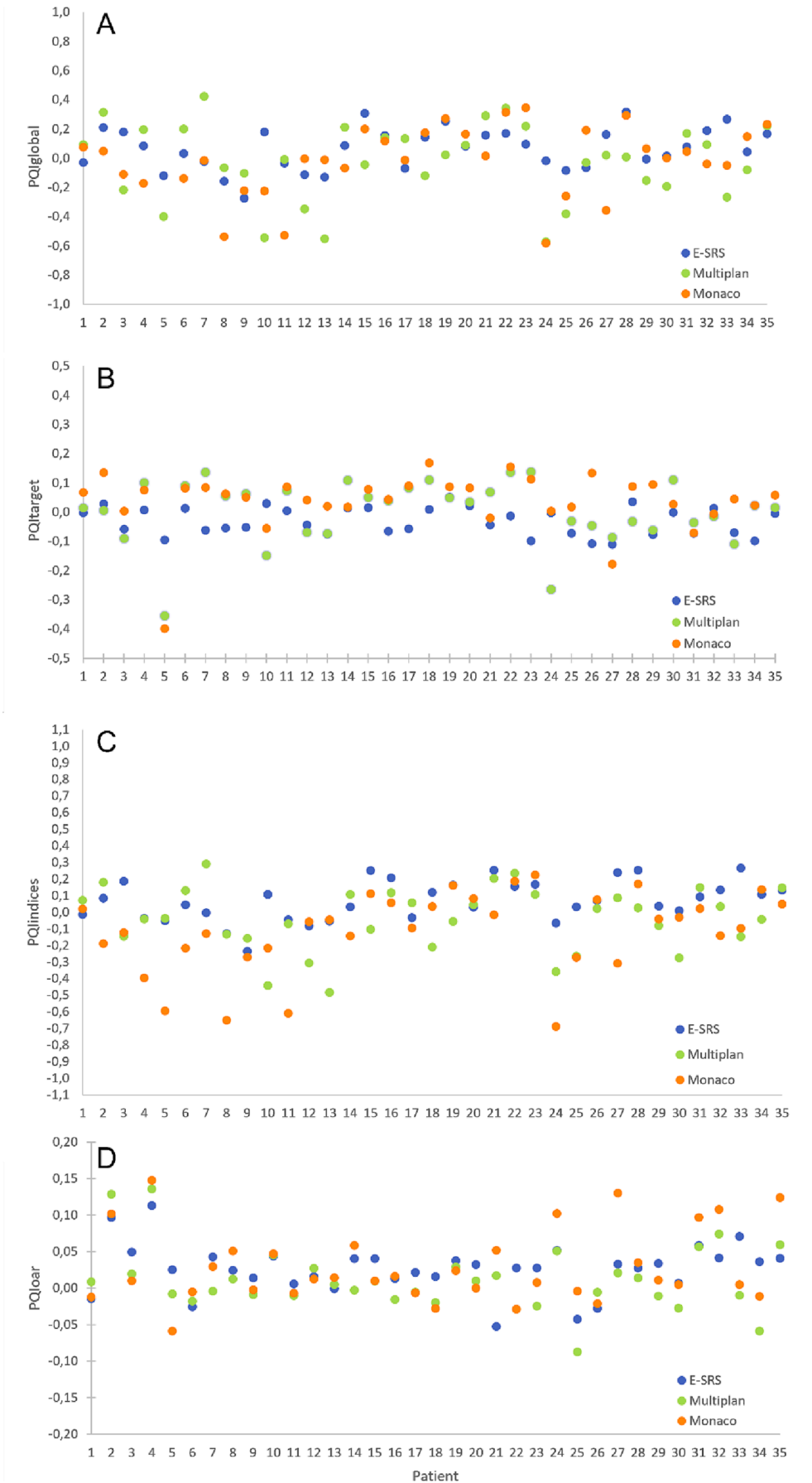


Fig. 3. PQI calculated for global plan quality scoring (A), target constraints achievement scoring (B), indices scoring (C) and OAR constraints achievement scoring.

3.2. QA results

VMAT E-SRS and Monaco plans QA results are shown in Table 7. Despite a number of MU up to 1.7 times higher with Monaco than with Elements Spine SRS, the MCS were found not to be statistically different. However, E-SRS plans generally resulted in lower MCS. Consequently, even if not statistically significant, the mean gamma passing rate was slightly lower for E-SRS (95.8%) compared with Monaco TPS (96.7%) using a 2%-2mm local analysis method. For Monaco TPS one single plan showed a gamma index < 95% (91.3%). Similarly, for Elements Spine SRS, for 3 patients, the gamma passing rate was comprised between 91.2 and 94.3%. However, all QA plans would have been validated in a clinical situation with global 3%-3mm gamma.

Table 7. Summary of QA and modulation complexity scores (MCS) results for 10 patients.

Analysis Criteria	E-SRS Mean [Range]	Monaco Mean [Range]	p-value
Mean Local Gamma Index 2%-2 mm	0.46 [0.41–0.53]	0.42 [0.35–0.49]	0.074
Mean Global Gamma Index 2% – 2 mm	0.39 [0.35–0.45]	0.35 [0.29–0.43]	0.123
Local 2% – 2 mm Gamma Index passing rate (%)	95.8 [91.2–98.3]	96.7 [91.3–99.3]	0.232
Global 2%-2mm Gamma Index passing rate (%)	97.4 [92.7–99.4]	97.9 [92.6–99.4]	0.770
MCS	0.25 [0.14–0.37]	0.27 [0.20–0.34]	0.432
MU	8323 [5775–12385]	12,008 [8017–20184]	0.002

4. Discussion

The main purpose of this study was to investigate for the first time the performances of a dedicated TPS performing SRS treatment plans delivered with a conventional Linac, compared to a dedicated Linac for the management of SRS, the Cyberknife and its TPS. The comparison was based on a cohort of 35 patients with spine tumours previously treated with the Cyberknife, in our institution. A comparison with Monaco TPS that we use routinely for our standard VMAT treatment was also performed.

Using VMAT delivery technique, E-SRS and Monaco TPS produced high quality plans with an achievement of our dosimetric goals comparable to the CyberKnife Multiplan TPS that was our “gold standard” modality. All plans were matching the dosimetric goals. The PTV coverage, D_{max} to the spinal cord, and conformation indices were generally found to be comparable between all modalities and the vertebral level did not have a significant impact on dosimetric results.

There was no significant difference between Monaco and Multiplan TPS treatment plans, with the exception of the PTV $D_{50\%}$ to the thoracic level, which was higher with Monaco. Hence, with Monaco TPS, we were able to mimic the quality of the plans obtained with Multiplan TPS. This was made possible because the prescription templates used in Monaco were based on the analysis of the dosimetric criteria collected from a large cohort of patients (>100) previously treated with the CyberKnife. Briefly, our prescription template was developed by considering a dose prescribed at the 80% isodose. The maximum dose allowed in the target was both considered as a constraint and as an objective. Finally, the prescribed dose to the CTV was generally 1.11 to 1.13 times higher than the dose prescribed at the 80% isodose

to match the $D_{50\%}$ generally obtained with the CyberKnife. Thus, although Monaco TPS is a VMAT dedicated TPS, initially designed to plan with homogeneity requirements specific to this technique, we showed that it was possible to develop prescriptions specific to SBRT which give similar dosimetric results to the CyberKnife technique [16], [17].

Conversely, the $D_{50\%}$ to the PTVs and CTVs were found significantly higher (up to 1.8 Gy higher) for E-SRS compared to Multiplan and Monaco treatment plans. The $D_{2\%}$ to the spinal cord was significantly lower with E-SRS than with Multiplan and Monaco, leading to a spinal cord DVH clearly favourable regarding the dose-volume constraints proposed in the literature [13], [14]. Thus, in the E-SRS optimization algorithm, a harder constraint was probably applied to the maximum dose to the spinal cord, compared with other TPS. This stricter competition between PTV and OAR combined with the use of conformation and gradient objectives in the prescription, may have played an important role in the increase of median dose to PTV and CTV observed on E-SRS plans. Note that the presence of these parameters did not result in statistically significant differences between TPS on the calculated PCI and GI indices.

The PQI calculations results were consistent with above observations. Although several dosimetric goals came from averaged Cyberknife's values obtained over all patients' cohorts, the PQIglobal scoring did not highlight a superiority of Cyberknife compared with both VMAT plans. Note that the goals and hypothesis made for PQI calculations may strongly impact the trends observed and are very subjective and dependant on the relative importance given to a constraint or to another, related to clinical practices. In our study, a weighting factor was affected to PTV $V_{100\%}$ only, as this criterion has the most relative importance in the clinical decision in our practice. In addition, PQIindices had the same relative importance than PQIoar and PQItarget in our PQIglobal calculations, as we considered pCi and GI metrics of importance for stereotactic plan evaluation. In an interesting way, the dispersion of the different PQIs observed for E-SRS plans was systematically smaller, suggesting a more reproducible planning strategy provided by automatization.

Several studies have compared the CyberKnife with VMAT for Spine SBRT planning, but, to our knowledge, this is the first time that a comparison is made with E-SRS TPS [4], [5], [18]. One study was performed on an anthropomorphic phantom and compared the Cyberknife technology to the Tomotherapy (Accuray, Sunnyvale, USA), Vero (Brainlab, Munich, Germany) and VMAT planning using Eclipse (Varian, Palo Alto, USA) and concluded that the Cyberknife had the sharpest dose falloff and achieved better plan quality for small targets [4]. In a multicentric study, 3 different patients with various spinal lesions were planned using the Tomotherapy and different VMAT planning solutions and compared to previously published Cyberknife benchmark data [5]. They concluded that VMAT plans were able to outperform these established Cyberknife benchmark data [19].

Several studies have compared E-SRS with other VMAT solutions [6], [7], [8], [9]. In a first study, similar dosimetric results were found on the dose to the spinal cord and to the PTV, when comparing the E-SRS with Eclipse TPS (AAA algorithm) [6]. The authors also noted an improvement of PCI and GI when using Elements Spine SRS, with the same beam geometry in both TPS but with duplication option in Spine SRS. In another study, the same TPS were compared, but using different algorithms for final dose calculation (AcurosXB for Eclipse TPS; Pencil Beam and MC algorithms for Spine SRS) [7]. Similar to us, they found a significant difference on spinal cord sparing, and on the maximum dose to the CTV with on average a maximum dose 1.6 Gy higher in Spine SRS using MC algorithm. Again, the same beam geometry was used in both TPS. However, contrary to us, similar PCI was found between their TPS used in routine for VMAT and both Element's algorithms. In another study, authors also compared Eclipse plans calculated with AcurosXB with E-SRS plans calculated with MC algorithm [8]. One major methodological difference between this study and others was that

planners were free to choose their ballistic in Eclipse (2 complete arcs with different collimator geometry), while E-SRS plans were computed with a defined geometry limited to one arc with duplication on. Similar to us and previous author's results, they found median doses to target volume 0.8 to 1.5 Gy higher in Spine SRS than in Eclipse, but they did not find a better spinal cord sparing with E-SRS and they conclude to an overall comparable plan quality between both TPS. Finally, *Saenz et al.* [9] compared E-SRS (MC) plans to Pinnacle (adaptive convolve algorithm) and Monaco plans (MC) and they found all their dosimetric criteria to be better achieved with Elements Spine SRS. In this study, target high dose was characterized by PTV $D_{5\%}$ and the three TPS were respecting the constraint of $D_{5\%} < 25$ Gy for 20 Gy prescribed dose. Contrary to other studies, the increase in the median dose to the targets observed with E-SRS was not observed here.

Thus, the increase in the median dose to PTV and CTV and spinal cord sparing in Spine SRS was a shared observation between most authors. However, we do not have any objective judgment about whether this dose increase to CTV and PTV should be clinically desirable or not, in a stereotactic prescription scheme, where maximal and median doses to the target volumes can vary considerably between centers using different prescription strategies. Spinal cord sparing is also a debatable question as the gradient augmentation has to be related to the patient repositioning and monitoring strategy and may expose to a higher risk of recurrence, even if an acute spinal cord sparing allows easier re-irradiation. In our institution, spinal cord sparing is not pushed as far as in Spine SRS, even with CyberKnife.

One of the factors that can influence the results is the inter-operator variability. As shown in a multi-institutional study focused on CyberKnife planning, a wide variability between treatment planning approaches and dosimetric results was observed between participants [19]. The plan quality dependence on planners' skill was also discussed elsewhere [18] and may have more impact than the TPS and treatment device combination. In this latter study, the authors proposed a crowd knowledge-based approach in spine stereotactic planning and showed this method to be effective in improving the global plan quality. To reduce plan quality dependence to user's skill, automated planning may be another promising solution.

As observed in our study, the PQI results were more homogeneous with the dedicated TPS than with manual planning solutions. The E-SRS is making a step in more reproducible plan solutions, integrating semi-automated planning, with a very limited number of parameters available for the operator, during the optimization process. The advantage of this TPS developed exclusively for SRS planning lies in its user-friendliness and its optimization of all phases, including: time-consuming delineation tasks simplified by anatomical libraries integrated into the software, allowing this phase to be automated [20], [21]; optimization constraints automatically managed once they are set by the user for each fractionation protocol. Furthermore, the optimization duplication option, which lead to the target subdivision into simpler volumes to avoid concavities/convexities, seems to allow a high level of spinal cord preservation.

When performing dosimetric studies, a particular attention should be paid to the tools used for the dose distribution comparison. In this study, a third-part software, MIM, with a systematic resampling in a 2 mm grid size, was used as unique tool to compare dose distributions. This methodology can lead to slight differences in DVH values observed in TPS and in MIM. In our results, this was particularly true for E-SRS plans, which have an adaptive sub-millimetric calculation grid, with a resampling of the grid depending on the size of the structure. Users should be aware of finer and non-isomorphic grids of Elements TPS. Using a unique software for dose distribution comparison allows to compare plans with the same tools, methods and resolution. Indeed, a study of *Stanley et al.* found differences in reported metrics for Elements, Eclipse, MIM, Raystation and Velocity when importing Dicom RTDose and RTStruct files in these different software [22]. Significant variations in volume calculations

were also observed elsewhere [23]. Resampling errors, which potentially occur when contour points from one treatment planning system are imported into another, can significantly affect volume calculations for small objects, and thus lead to discrepancies in DVH calculation and plan comparison.

Another element to consider in this study was that the comparison between dose distributions was computed with different algorithm classes. Indeed, Monaco and E-SRS dose distribution were computed with a MC algorithm, whereas Multiplan dose distribution was computed with the RT algorithm. It has been demonstrated that MC algorithms provide a higher accuracy in dose calculation in heterogeneous medium and are recommended for stereotactic treatment planning [17]. Hence, in two previous studies, RT and MC algorithms were compared for Cyberknife' spine planning. *Li et al.* observed differences in PTV coverage from 1% in cervical region up to 13% in thoracic region [24]. The dose to the spinal cord found with MC algorithm was generally lower than with RT algorithm. Similarly, *Okoye et al.* found a significant loss of PTV coverage when recalculating in MC thoracic spinal plans optimized in RT [25]. Finally, both authors concluded in the necessity to use MC algorithm for thoracic spinal lesions planning. In our study, MC was not clinically implemented at the time the plans were performed. The goal of this study was not to evaluate the accuracy of the algorithms but to compare the optimization results produced by three TPS, and to assess the E-SRS automatic planning performances. However, a study conducted in parallel allowed us to obtain the same trends mentioned by the two previous studies. In this study, the Cyberknife plans were retrospectively recomputed with an independent MC dose engine (Surecalc v. 7.3.1; scimoca 1.7.1.5050 dose engine (MIM software Inc., Cleveland, USA)). We observed that PTV coverage and OAR D_{max} were overestimated with the RT algorithm, whatever the vertebral level (Fig. 1 - Supplementary Material). PTV $V_{100\%}$ was found to be on average 10%, 15% and 5% lower for cervical, thoracic and lumbar vertebral level, respectively, with MC calculations compared with RT. $D_{2\%}$ to spinal cord followed the same trend, with an average dose reduction of up to 8% to the thoracic level.

In the present study, we observed that E-SRS plans resulted in a significantly lower number of MU and in a lower MCS compared to Monaco TPS but without compromising the plan delivery quality. Compared with Multiplan TPS, the number of MU obtained for the plans performed with E-SRS and Monaco TPS were significantly lower, which resulted in an improved delivery efficiency for an equivalent plan quality compared with our gold standard. This also resulted in an important decrease of the beam on time for the VMAT technique compared with the Cyberknife. This was estimated to 6 min, 10 min and 40 min, for Elements Spine SRS, Monaco and Cyberknife treatments, respectively.

Finally, the CyberKnife clinical plans were performed using fixed cones. Since then, our CyberKnife was changed for a S7 model implying changes in our planning method and delivery for spine SBRT, i.e the use of VOLO optimization algorithm (Precision, Accuray, Sunnyvale) and the IRIS as beam collimation. These recent features added to Cyberknife linac and TPS optimize the beam arrangement, decrease the beam on time and the number of MU [26], [27]. Furthermore the use of the MLCincise could contribute to a treatment delivery time decrease of 30% compared to fixed cones [28]. However, our goal in this study was to assess E-SRS performances for spinal SBRT automatic planning compared to plans produced by skilled users on other TPS, based on our clinical background.

5. Conclusion

Spinal SBRT planning with E-SRS offers very qualitative dosimetric solutions, close to our clinical experience with both Multiplan and Monaco TPS. There is a slightly different balance between goals to spinal cord sparing and PTV doses between our traditional way of prescribing in our clinical TPS and the natural Spine SRS optimizer behaviour but, to date, there is no any objective judgment about whether these differences are clinically desirable or not, in a stereotactic prescription scheme. Finally, the E-SRS special approach offers a very effective and user-friendly semi-automated planning tools and is secure and promising for linac-based spinal SBRT.

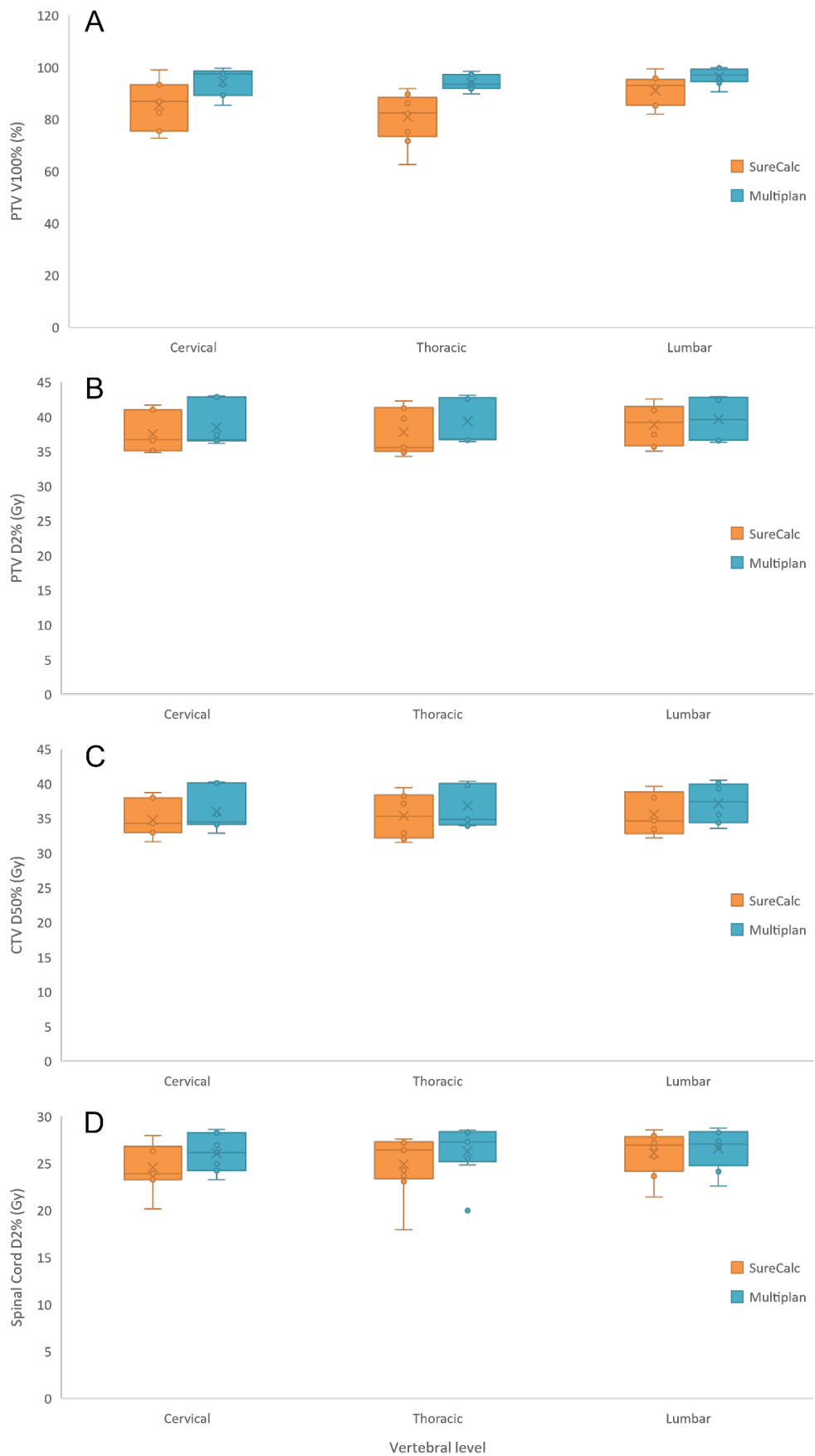
Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: This work was performed in the framework of a research cooperation agreement with Brainlab society.

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Appendix A. Supplementary data



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