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Research Article

Dosimetric Comparison of SEQ versus SIB-VMAT in the Treatment of Esophageal Cancer

Azhar Rashid[1*], Rabia Khalil[2], Zainab Rafat Ali[3], Erum Idrees[4], Muhammad Ali Memon[5]
[1*]Department of Clinical and Radiation Oncology, Neurospinal and Cancer Care Institute (NCCI), Karachi, Pakistan.
[2]Medical Physicist, Neurospinal and Cancer Care Institute Karachi (NCCI), Karachi, Pakistan.
[3,4]Postgradate Resident, Radiation Oncology, Neurospinal and Cancer Care Institute (NCCI), Karachi, Pakistan.
[5]Oncologist, Clinical and Radiation Oncology, Neurospinal and Cancer Care Institute (NCCI) Karachi, Pakistan.
Corresponding Author: Azhar Rashid
Department of Clinical and Radiation Oncology, Neurospinal and Cancer Care Institute (NCCI) Karachi, Pakistan.
Email: azhar_rashid@hotmail.com
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ABSTRACT
Background: Esophageal cancer carries a high global mortality burden. Two dose-escalation techniques are available with VMAT-based radiation therapy: sequential boost (SEQ) and simultaneous integrated boost (SIB). However, there is little direct dosimetric comparison of these methods in esophageal cancer.
Objective: This study aimed to compare SEQ-VMAT and SIB-VMAT in locally advanced esophageal cancer using OAR dosage parameters, conformity index (CI), and homogeneity index (HI).
Methods: Ten patients with histopathologically proven locally advanced esophageal cancer were included in this retrospective dosimetric study: SEQ-VMAT (n=5) and SIB-VMAT (n=5). SEQ delivered 45 Gy/25 fx, followed by a boost to 50.4 Gy/28 fx; SIB delivered 50.4 Gy (1.8 Gy/fr) to GTV and 45 Gy (1.61 Gy/fx) to PTV concurrently in 28 fractions. DVH-based dosimetric parameters (CI, HI, V95%, OAR doses) were analyzed against QUANTEC tolerances. Statistical analysis was performed using SPSS v25.0 ($p<0.05$).
Results: Both techniques achieved adequate PTV coverage (median V95% 96.1% vs. 95.5%). SIB-VMAT showed significantly better conformity (CI 0.90 vs. 0.76, $p=0.012$) and significantly lower left lung mean dose and V20 (both $p<0.02$), whereas SEQ-VMAT showed significantly better homogeneity (HI 0.08 vs. 0.15, $p=0.021$). All other OAR doses were statistically equivalent between the groups and within the QUANTEC tolerances.
Conclusion: Both SEQ-VMAT and SIB-VMAT achieved adequate target coverage and kept organ-at-risk doses within QUANTEC-based tolerances for locally advanced esophageal cancer. SIB-VMAT showed significantly better conformity and lower left lung dose, whereas SEQ-VMAT showed significantly better dose homogeneity; other organ-at-risk parameters were statistically equivalent between the two techniques. Given this trade-off, its shorter overall treatment course, and the small sample size studied, SIB-VMAT may be considered a practical alternative to SEQ-VMAT, though larger studies are needed before either technique can be recommended as preferred.

Keywords: Esophageal Cancer, VMAT, Simultaneous Integrated Boost (SIB), Sequential Boost (SEQ), Conformity Index, Homogeneity Index, Organs at Risk, Dosimetric Comparison, Radiotherapy.

INTRODUCTION

Esophageal cancer is one of the most lethal malignancies worldwide. GLOBOCAN 2022 estimates place the global burden at approximately 511,000 new cases and 445,000 deaths annually, with an age-standardized incidence rate of 5.00 and a mortality rate of 4.30 per 100,000 person-years [1]. Despite advances in diagnosis and multimodal therapy, local recurrence after definitive chemo radiotherapy remains high (40–60 %), with a 5-year overall survival of only 10–30% [2]. For patients with inoperable or unresectablelocally advanced disease, definitive concurrent chemoradiotherapy is the recommended standard of care, a position established by the landmark RTOG 85-01 trial [3], which demonstrated that radiotherapy combined with concurrent 5-fluorouracil and cisplatin produced long-term survival comparable to that achieved with surgery alone [3].

Radiotherapy delivery techniques have evolved considerably to improve the therapeutic ratio. Intensity-modulated radiotherapy (IMRT) improves the conformity of the target volume and sparing of organs at risk compared with older conformal techniques [4], and volumetric-modulated arc therapy (VMAT), a more advanced form of IMRT, has shown equivalent or superior dose distribution with decreased organ-at-risk dose and shorter delivery time [4]. Within the VMAT-based planning, dose escalation to the gross tumor volume can be achieved through two distinct strategies. In the sequential boost (SEQ) approach, an initial course covering the elective/nodal volume is followed by a separate boost phase to gross disease, whereas in the simultaneous integrated boost (SIB) approach, differential dose levels are delivered to multiple target volumes within the same treatment fraction, allowing dose escalation to the tumor while shortening overall treatment time [5].

Comparative data on SEQ versus SIB delivery exist for several disease sites. In head and neck cancers, SIB enables differential dosing within a single plan and potentially shorter treatment time but typically delivers higher biologically effective doses to elective nodal regions than SEQ [6]. Both approaches are generally regarded as producing comparable outcomes, with the choice of technique often being a subjective or dosimetrically driven decision [7]. In breast cancer, SIB has shown better conformity and less dose spillage beyond the boost volume compared with sequential boost, without increasing the dose to organs at risk [8]. In trimodal therapy for bladder cancer, SIB and SEQ-VMAT are both widely used; however, evidence directly comparing their dosimetric performances remains limited [5].

In esophageal cancer specifically, dosimetric evidence is more fragmented. Existing studies have largely compared delivery platforms — IMRT, VMAT, and helical TomoTherapy — for SIB plans across different tumor locations, finding that the optimal technique varies by tumor site, with IMRT preferred for upper and middle thoracic disease due to superior conformity and reduced cardiac dose, and helical TomoTherapy favored for cervical esophageal tumors [9]. However, a direct comparison of the SEQ and SIB boost strategies within VMAT — evaluating plan quality (conformity index, homogeneity index, organ-at-risk sparing against QUANTEC-based tolerances [10])–has not been well characterized for esophageal cancer, unlike in head and neck, breast, or bladder malignancies where such comparisons already exist.

This gap is clinically relevant because thoracic organs at risk in esophageal radiotherapy (lung, heart, and spinal cord) carry well-defined dose tolerances [10], and treatment schedule length has direct implications for patient burden and departmental throughput. Establishing whether SIB-VMAT can match or improve upon SEQ-VMAT's dosimetric and clinical performance, while shortening the overall treatment time, would provide practical guidance for technique selection in routine practice.

This retrospective dosimetric study was undertaken to directly compare SEQ-VMAT and SIB-VMAT in patients with locally advanced esophageal carcinoma, evaluating target coverage, conformity index, homogeneity index, and organ-at-risk doses against QUANTEC tolerances to inform boost-technique selection in esophageal cancer radiotherapy.

MATERIALS AND METHODS

Patient Selection and Simulation

Ten patients diagnosed with locally advanced esophageal carcinoma by a radiation oncologist were selected for this retrospective dosimetric study and were divided equally into sequential boost VMAT (SEQ-VMAT, n=5) and simultaneous integrated boost VMAT (SIB-VMAT, n=5) groups. The patients were positioned supine with both arms raised above the head and immobilized using a wing board. CT simulation with contrast was performed with 2 mm axial slice thickness, and images were exported to the contouring workstation.

Contouring

The gross tumor volume (GTV) included the primary esophageal tumor and involved regional lymph nodes, delineated using contrast CT findings. The clinical target volume (CTV) was generated by adding a craniocaudal and radial margin to the GTV to encompass elective nodal regions at risk; a uniform margin was added to generate the planning target volume (PTV). The bilateral lungs, heart, spinal cord, and liver were contoured as organs at risk (OARs).

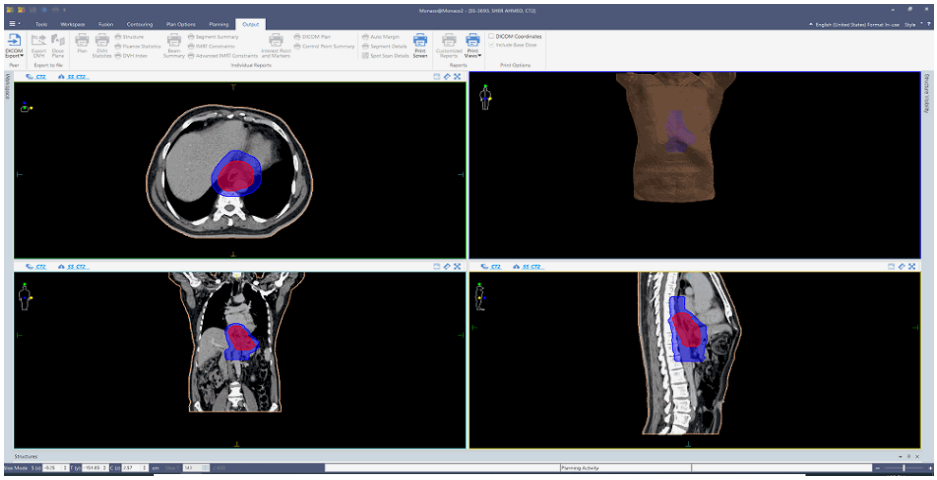

Figure 1: Contours of Esophageal Tumor

Dose Prescription

The patients were treated with either SEQ-VMAT (n=5) or SIB-VMAT (n=5). In the SEQ-VMAT group, 45 Gy was delivered in 25 fractions to the elective volume, followed by a sequential boost to a cumulative dose of 50.4 Gy in 28 fractions for the gross disease. In the SIB-VMAT group, 50.4 Gy (1.8 Gy/fraction) was concurrently delivered to the GTV and 45 Gy (1.61 Gy/fraction) to the PTV within a single plan, over 28 fractions.

Treatment Planning

Plans were generated for each patient using the Monaco TPS (version 6.1.3.0, Monte Carlo algorithm) with the VMAT technique on a single isocenter encompassing the thoracic target volumes, with 6 MV coplanar arcs. Each isocenter used one beam with two arc rotations (clockwise and counter-clockwise), optimized to achieve adequate PTV coverage while minimizing the dose to the lungs, heart, and spinal cord. For SEQ-VMAT, a two-phase prescription was used: 45 Gy in 25 fractions to the elective volume (Phase I), followed by a sequential boost of 5.4 Gy in 3 fractions to gross disease (Phase II), for a cumulative dose of 50.4 Gy in 28 fractions. For SIB-VMAT, a single-phase concurrent prescription delivered 50.4 Gy (1.8 Gy/fraction) to the GTV and 45 Gy (1.61 Gy/fraction) to the PTV simultaneously over 28 fractions. Plans were normalized such that at least 95% of the PTV received the prescribed dose.

Plan Evaluation Parameters

Plan quality was assessed against the ICRU Report 50 criterion for target coverage (minimum PTV dose ≥95% and maximum dose ≤107% of the prescription) and QUANTEC-based OAR dose-tolerance guidelines (Table 1). Four indices were used to characterize the target volume dosimetry:

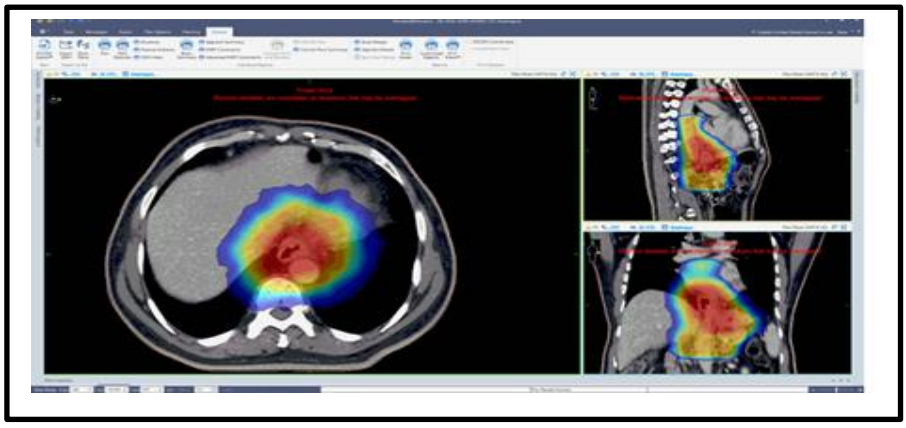

Figure 2: Isodoses of Simultaneous Integrated Boost

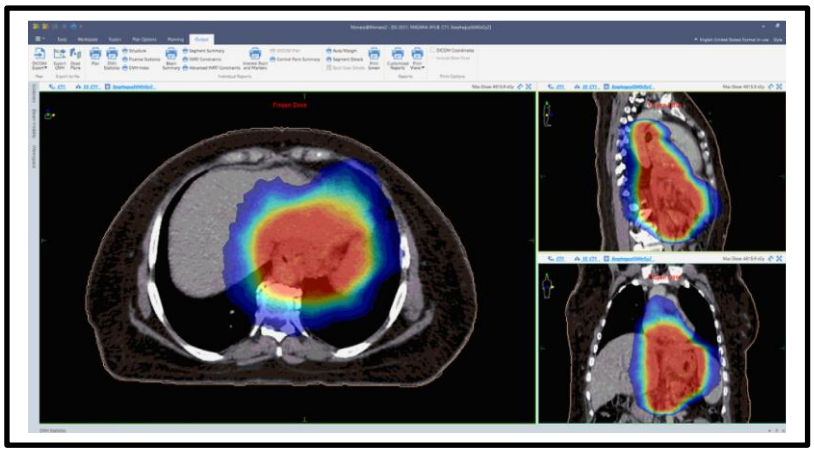

Figure 3: Isodoses of Sequential

Homogeneity Index (HI):

$$\mathbf{HI} = \frac{D_2 - D_{98}}{D_P}$$

Where D_2 and D_{98} are the doses received by 2% and 98% of the PTV, respectively, and Dp is the prescribed dose. Values closer to zero indicate a more uniform dose distribution.

Conformity Index (CI):

$$CI = \frac{V_{RI}}{TV}$$

where VRI is the volume of the reference (prescription) isodose and TV is the total PTV. Values closer to 1 indicate better conformity.

OAR doses were evaluated using maximum and mean doses against the tolerance limits summarized in Table 1.

Table1. OAR Dose Tolerance Constraints Were Used for Plan Evaluation:

Organ at Risk	Tolerance Dose	Organ at Risk	Tolerance Dose
Lung (bilateral)	Dmean <20 Gy; V20 <30–35%	Liver	Dmean <30 Gy; V30 <60%
Heart	V30 <40–46%; Dmean <26 Gy	Kidney (bilateral)	Dmean <18 Gy; V20 <32%
Spinal Cord	Dmax <45–50 Gy	Bowel	Dmax <54 Gy; V45 <195 cc

RESULTS

Target Coverage and Plan Quality Indices

Both techniques met the ICRU Report 50 target-coverage criterion (≥95% of the prescription dose), with no significant difference in PTV/GTV V95% or GTV Dmax (Table 2). SIB-VMAT showed significantly better conformity (CI: 0.90 vs. 0.76, p = 0.012), while SEQ-VMAT showed significantly better homogeneity (HI: 0.08 vs. 0.15, p = 0.021).

Table 2. Target Coverage and Plan Quality Indices, SIB-VMAT vs. SEQ-VMAT (Median, Range).

Parameter	SIB-VMAT (n=5)	SEQ-VMAT (n=5)	p-value*
PTV V95% (%)	96.1 (94.5–97.3)	95.5 (94.8–97.9)	0.548
GTV V95% (%)	95.4 (95.0–98.0)	96.4 (95.7–99.3)	0.095
GTV Dmax (cGy)	5274 (5234–5348)	5278 (5236–5321)	0.841
Conformity Index (CI)	0.90 (0.86–0.93)	0.76 (0.70–0.84)	0.012†
Homogeneity Index (HI)	0.15 (0.12–0.30)	0.08 (0.06–0.13)	0.021†

*Mann-Whitney U test (two-tailed). †Statistically significant, p < 0.05.

Organ-at-Risk Doses versus QUANTEC Tolerances

SIB-VMAT achieved a significantly lower left lung mean dose (9.6 vs 16.4 Gy, p = 0.016) and V20 (14.0% vs. 26.3%, p = 0.008), with a similar non-significant trend for the right lung (p = 0.056 for both). No other OAR parameter (kidney, heart, spinal cord, liver) differed significantly between groups, and all median OAR values remained within QUANTEC tolerances (Table 3). Bowel V45 could not be tested statistically because of insufficient data (n=3 SIB, n=1 SEQ), but the available values were within tolerance.

Table 3. Organ-At-Risk Dose Comparison, SIB-VMAT vs. SEQ-VMAT (Median, Range)

Organ	Parameter	SIB-VMAT	SEQ-VMAT	p-value*	QUANTEC Tolerance
Kidney LT	Mean dose (Gy)	8.27 (3.33–13.86) n=5	5.47 (3.14–17.01) n=4	0.730	Dmean < 18 Gy
Kidney RT	Mean dose (Gy)	4.61 (0.80–7.42) n=5	5.04 (1.83–9.38) n=4	0.730	Dmean < 18 Gy
Lung LT	Mean dose (Gy)	9.56 (7.89–12.79)	16.36 (12.39–18.47)	0.016†	Dmean < 20 Gy
Lung LT	V20 (%)	14.0 (11.4–16.7)	26.3 (20.8–37.0)	0.008†	V20 < 30–35%
Lung RT	Mean dose (Gy)	9.15 (6.32–10.84)	16.14 (7.97–16.78)	0.056	Dmean < 20 Gy
Lung RT	V20 (%)	8.43 (2.53–10.74)	20.20 (7.06–24.04)	0.056	V20 < 30–35%
Heart	Mean dose (Gy)	21.38 (19.33–30.20)	24.00 (15.83–30.81)	1.000	Dmean < 26 Gy
Heart	V30 (%)	21.95 (16.05–42.14)	21.16 (12.53–44.61)	0.548	V30 < 40–46%
Spinal Cord	Max dose (Gy)	26.54 (20.05–27.17)	29.77 (21.32–37.01)	0.222	Dmax < 45–50 Gy
Liver	Mean dose (Gy)	17.22 (6.83–20.03)	19.70 (11.41–24.85)	0.548	Dmean < 30 Gy
Bowel	V45 (cc)	16.09 (14.11–32.50) n=3	20.19 n=1	n/a	V45 < 195 cc

*Mann-Whitney U test (two-tailed). †Statistically significant, p < 0.05.

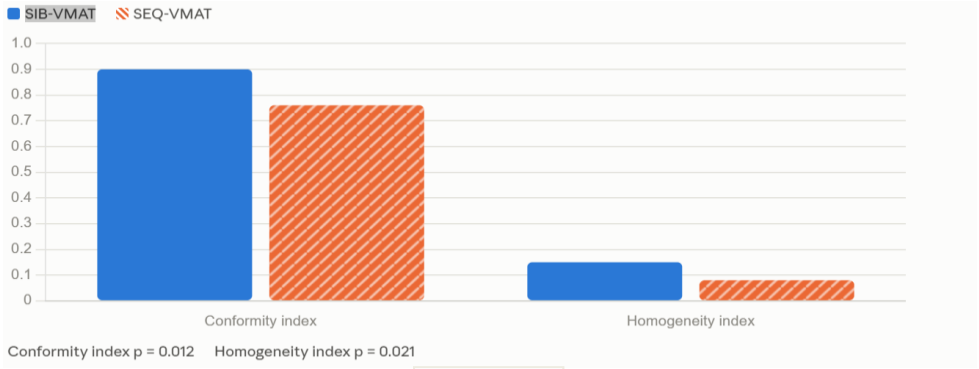

Figure 3

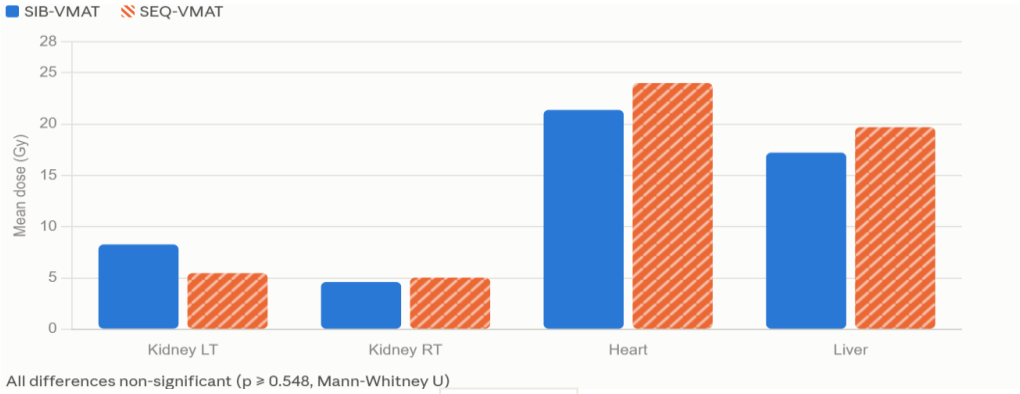

Figure 4

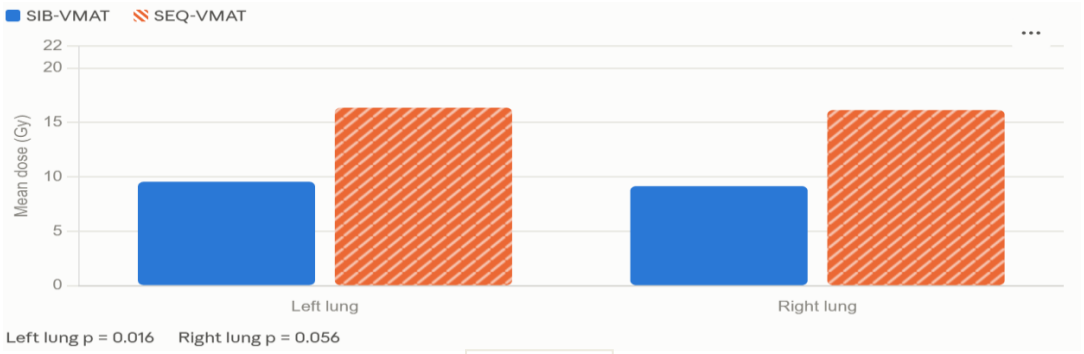

Figure 5

DISCUSSION

Both SEQ-VMAT and SIB-VMAT achieved adequate PTV/GTV coverage per ICRU Report 50 criteria, with no significant difference in target coverage or GTV Dmax. However, the plan-quality indices showed a reciprocal pattern: SIB-VMAT produced a significantly higher conformity index, while SEQ-VMAT produced a significantly lower (more favorable) homogeneity index. This trade-off likely reflects the underlying planning approach: SIB's single concurrent-dose-level optimization favors conformity around the boost volume, whereas SEQ's independently optimized phases favor a more uniform dose distribution, a pattern consistent with prior SIB-vs-SEQ comparisons in breast cancer [8].

SIB-VMAT also achieved significantly lower mean left lung dose and V20, with a similar but non-significant trend for the right lung, while heart, kidney, spinal cord, and liver doses were statistically equivalent between groups and within QUANTEC tolerances in both arms. This lung-sparing advantage, together with a shorter overall treatment course — dose escalation is completed within the same 28-fraction schedule rather than an appended boost phase–supports SIB-VMAT as a practical alternative to SEQ-VMAT, particularly where improved conformity and shorter treatment duration are desired for locally advanced esophageal cancer, provided its modestly higher dose heterogeneity is acceptable at planning.

These findings should be interpreted cautiously, given the small sample size (n=5 per arm), which limited the power for several comparisons (notably the right lung and bowel dose) and precluded correction for multiple testing across 16 parameters. The retrospective design could not account for inter-patient variations in tumor location or anatomy. Larger prospective studies with larger cohorts are needed to confirm whether these dosimetric findings are more broadly applicable.

CONCLUSION

In this comparative dosimetric analysis, both SEQ-VMAT and SIB-VMAT achieved adequate target coverage for locally advanced esophageal cancer, with organ-at-risk doses remaining within QUANTEC-based tolerance limits in both groups. SIB-VMAT offered significantly better conformity and lower lung dose, whereas SEQ-VMAT offered significantly better dose homogeneity. No other dosimetric parameter differed meaningfully between the two techniques. Given this trade-off and the small sample size of the present study, SIB-VMAT may be considered a practical alternative to SEQ-VMAT that additionally allows dose escalation within a single, shorter treatment course. However, larger prospective studies are needed before either technique can be recommended as the preferred standard.

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