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# Outcomes of Single Fraction Stereotactic Ablative Radiotherapy for Lung Metastases

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Stereotactic Ablative Radiotherapy (SABR) has been previously investigated as an alternative to thoracic surgery in patients with a limited number of pulmonary nodules from different primary tumors. We here report the clinical outcomes of a series of consecutive patients homogenously selected and treated with single dose SABR in our Institution. Eligibility criteria were: 1-5 lung metastases, maximum tumor diameter $<$50 mm, absent or controlled extra-thoracic disease, adequate pulmonary function, no prior radiotherapy, performance status ECOG 0-1. All patients were treated with a single dose of 26 Gy prescribed to the 80% isodose, by 3D-CRT or by IGRT-VMAT. Follow-up consisted of clinical evaluation and periodic CT scans. Primary endpoints were Local Control (LC), toxicity and Progression-Free Survival (PFS). Secondary endpoints were Cancer-Specific Survival (CSS) and Overall Survival (OS). Out of 102 patients treated with SABR between october 2003 and october 2011, we selected 67 patients for a total of 90 lesions. Main primary tumor sites were lung and colon-rectum (37.3% and 43.3% of lesions, respectively). Median follow up time was 24 months. Treated metastasis progression at SABR site was observed in 10 lesions (11.1%), and actuarial LC rates at 1 and 2 years were respectively 93.4% and 88.1%. Systemic failure occurred in 37 patients (55.2%) at a median interval of 8 months after SABR. PFS rates were 72% and 55.4% at 1 and 2 year. Seven patients had grade 1 (10.4%) and 8 grade 2-3 late radiological toxicity (11.9%), while 6 experienced late chest wall toxicity (2 rib fractures, 4 chronic chest pain, 8.9%). CSS rates at 1 and 2 years were 90% and 76%, while OS rates were 85.1% and 70.5%, respectively. Median survival time was 40 months. On multivariate analysis, a disease-free interval longer than 24 months was close to significance for a benefit in CSS ($p = 0.07$; HR 0.34 [95% CI 0.1-1.12]). The study includes a cohort of patients treated with single fraction 26 Gy SABR followed for a prolonged time interval. Single fraction SABR appears to be an effective treatment option, with little observed acute toxicity and limited late toxicity ($<$15%); its advantages also include a high patients' compliance, a short overall treatment time and an easy combination with systemic therapies. These results might provide supportive evidence to the use of single fraction SABR as a valid and acceptable alternative to surgery for pulmonary metastases from different primary tumors.

Key words: Stereotactic radiotherapy; Lung metastases; Radiosurgery.

## *Introduction*

Lung metastases are a quite common event in solid tumors (1), frequently diagnosed in the course of regular follow-up in asymptomatic patients, without evidence of any other disease site or with a controlled primary tumor and/or other controlled metastatic lesions. Patients affected with 1-5 metastatic pulmonary nodules might be in a condition recently defined as oligo-metastatic disease (2, 3), and are often treated with a combination of systemic and

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metastasis-directed therapies (2-5). Surgical removal of limited pulmonary metastases usually is the first therapeutic option (6), and radiation was rarely used until recent years, when the emerging alternative represented by Stereotactic Ablative Radiation Therapy (SABR) has been considered with increasing interest, as potentially equally effective and less toxic, especially in elderly patients or in patients with important comorbidities. SABR is treatment technique characterized by a very sharp dose gradient, which allows the delivery of high doses per fraction in few days, corresponding to consistently higher biologically equivalent doses in comparison with standard radiotherapy. It has been proven to be an effective treatment modality in terms of tumor control in early stage non-small cell lung cancer and it has been extended to lung metastases, with promising results in increasing progression-free survival. These findings are still not fully validated, as they mainly come from uncontrolled non-randomized studies with the primary endpoint of local control, and a miscellaneous cohort of patients has been recruited so far (5). In most of the clinical trials, SABR was delivered in few fractions (3-10), with a local control probability at 1 year in the range 70-90% (7-10). Single fraction SABR has been less investigated (11, 12), even if it is attractive for several clinical considerations: high patients' compliance and acceptance of treatment, the possibility to treat more than 1 lesion in few days, the lower cost, the lower machine workload and an easier combination with systemic therapies.

Since the start of the SABR program for lung metastases in our Institution we gradually implemented this strategy, and we previously reported on a series of patients treated with a combination of fractionated and single fraction SABR (9). Purpose of this report was to selectively analyze clinical outcomes of single fraction SABR in a larger series of patients with a longer follow-up interval.

## *Materials and Methods*

### *Patients*

Clinical selection criteria for SABR were: 1 to 5 lung metastases, maximum tumor diameter smaller than 50 mm, absent or controlled extra-thoracic disease, adequate pulmonary function ($FEV_1$ higher than 40% predicted and DLCO higher than 40% predicted), no prior radiotherapy, performance status ECOG 0-1. Patients with any primary tumor histology were eligible (except those with germ cell tumors or hematological malignancies). All patients included in the present study were mandatorily restaged according to clinical guidelines for their primary tumor prior to SABR; a PET-CT scan was always requested to complete restaging when not previously performed (the interval between PET scan and SABR was in the range 20-60 days).

**Table I**
Patients' characteristics.

| | |
|---|---|
| No. of patients | 67 |
| No. of lesions | 90 |
| Age (years) | |
| Median (range) | 71 (40-86) |
| Male:female proportion | 1.91:1 |
| Primary tumor | |
| NSCLC adenocarcinoma | 10 (15%) |
| NSCLC squamous | 7 (10.4%) |
| NSCLC NOS/other | 8 (12%) |
| CRC | 27 (40.3%) |
| Melanoma | 5 (7.5%) |
| Head and neck | 3 (4.5%) |
| HCC | 2 (2.9%) |
| Esophagus | 2 (2.9%) |
| Breast | 1 (1.5%) |
| Kidney | 1 (1.5%) |
| Prostate | 1 (1.5%) |
| Disease-free interval (months) | |
| Median (range) | 26 (1-129) |
| Prior systemic therapy for metastatic disease | |
| Yes | 17 (25.3%) |
| No | 50 (74.7%) |
| No. of metastases | |
| 1 | 46 (68.7%) |
| 2 | 19 (28.3%) |
| 3 | 2 (3%) |
| Tumor size (mm) | |
| Median (range) | 17 (7-38) |
| Gross tumor volume (cc) | |
| Median (range) | 2.1 (0.18-28.4) |

Abbreviations: NSCLC: Non-Small Cell Lung Cancer; CRC: Colo-Rectal Cancer; HCC: Hepatocarcinoma.

Lung metastases were clinically diagnosed without a histological confirmation in the majority of patients (89.5%). Metastatic lesions were defined as the onset of new lung nodules ≥8 mm of diameter, with $^{18}$FDG uptake and a standard uptake value >4.5, during the regular follow-up of a previous cancer disease. Patients with central metastatic lesions (<2 cm from trachea, main bronchi and/or great vessels) were excluded. Patient's characteristics are summarized in Table I.

Written informed consent for SABR was obtained from every patient.

### *Treatment Technique*

Patients were either treated with 3D-CRT, or with IGRT-VMAT. For 3D-CRT, each patient was immobilized in supine position with a stereotactic body frame (SBF-ELEKTA® Oncology Systems), with a diaphragm compression device to reduce tumor's motion. Set-up was checked using a laser system and permanent skin markers. A planning CT scan of the entire thorax (2.5 mm thick slices) without intravenous contrast media was obtained, with CT acquisition time of 3 seconds to include all phases of one respiratory cycle. The target was outlined in sequential axial CT images and the Gross Tumor Volume (GTV) contoured using a CT lung window setting (1600-400 Hounsfield units). Clinical Target Volume (CTV) corresponded to GTV, as previously reported. The Planning Target Volume (PTV) was generated adding a 5 mm margin in the axial plane and a 10 mm margin in the longitudinal direction, in order to compensate for set-up errors and organ motion. A Multi-Leaf Collimator–PTV distance of 3-5 mm was used to adequately cover PTV within 80% isodose. Adjacent organs-at-risk (esophagus, heart, spinal cord, both lungs, and trachea-main bronchi) were then outlined. OTP Oncentra Masterplan® version 1.5 software was used for treatment planning and convolution superposition (collapsed cone) algorithm was used for dose calculation. SABR was delivered with an Elekta Precise™ linear accelerator, using 6 to 8 static non-opposing, non-coplanar shaped fields, with 6-10 MV photons; treatment time was around 30 minutes. Orthogonal anterior (0°) and lateral (90°) digital portal images were obtained and compared to Digitally Reconstructed Radiographs (DRRs) before each treatment session.

For IGRT-VMAT, a frameless Bluebag® vacuum-pillow was used as immobilization device, and an Internal Target Volume (ITV) was defined in which the GTV included the tumor position in all phases of the normal respiratory cycle, outlined using a CT windows setting. The ITV was expanded by 3 mm to create the PTV. Monaco™ software was used for treatment planning and Monte Carlo algorithm for dose calculation. Treatments were delivered with an Elekta Axesse ™ Linear Accelerator, with 6-10 MV photons and treatment time of about 20 minutes. Before treatment delivery, image guidance using cone-beam CT was used to localize the target.

For all patients, a dose of 26 Gy was prescribed to the PTV encompassing 80% isodose, with normalization to 100% at the isocenter, corresponding to a minimal Biologically Effective Dose of 94 Gy at the tumor periphery with an alfa/beta ratio of 10 Gy ($BED_{10}$) and of 138 Gy at isocenter.

Dose limits to organs-at-risk were described previously (9) and were as follows (converted in 2 Gy-equivalent according to Linear Quadratic Model): ipsilateral Mean Lung Dose $< 15\,Gy_2$ (radiation pneumonitis, alfa/beta = 3.5 Gy), spinal cord $< 36\,Gy_2$ (alfa/beta = 2 Gy), skin $< 56\,Gy_2$ (necrosis, alfa/beta = 2.5 Gy), trachea/main bronchi $< 78\,Gy_2$ (stenosis/fistula, alfa/beta = 3 Gy), heart $< 70\,Gy_2$ (pericarditis, alfa/beta = 4 Gy).

Median radiation delivery time with 3DCRT was 30 minutes, with VMAT 18 minutes (range 15-21).

*Follow-up and Statistics*

Primary endpoint of this study was Local Control (LC); secondary endpoints were Progression-Free Survival (PFS), Cancer-Specific Survival (CSS), Overall Survival (OS) and treatment-related toxicity.

All patients underwent clinical examination and CT scan for evaluation of treatment results and side effects 6 weeks after SABR, and were then prospectively followed with clinical examination and CT scans every 3 months. CT-PET was used in follow-up only in case of differential diagnosis between radiation fibrosis and tumor progression.

Median follow-up time was calculated with reverse Kaplan-Meier method.

Lung toxicity was graded according to the RTOG acute radiation toxicity score (for events occurring between day 1 and day 90 from the start of radiation treatment) and to the RTOG late radiation toxicity score (for events occurring after day 90) (http://www.rtog.org/members/toxicity).

Local tumor control was defined as the absence of local progression, evidenced by tumor growth or re-growth after initial shrinkage. Tumor recurrence was considered if a solid homogeneous mass increasing in size during follow-up was evident.

Cox proportional hazards model was used to calculate the Hazard Ratios (HRs) and their 95% confidence interval in multivariate analysis. All $p$ are two-sided and $< 0.05$ was considered for statistical significance. The proportionality assumption was investigated using a test based on the Schoenfeld residuals. Factors investigated for prognostic value with respect to clinical outcome parameters were: age, gender, primary tumor site (lung vs. other, colo-rectal vs. other), disease-free interval (median time from primary tumor diagnosis and lung systemic spread), prior local therapy, presence of other controlled metastases (by other metastasis-directed therapies or by systemic therapies), number and size (GTV) of lesions and other local ablative treatments at disease progression after SABR (when progression was limited to <3-5 lesions). Performance status was not considered since patients were strictly selected from a clinical point of view (only ECOG 0-1).

Survival curves were generated using the method of Kaplan and Meier starting from time of SABR, and were defined as follows: LC (event: local recurrence at SABR site, per lesion), PFS (event: local and/or nodal and/or systemic failure), CSS (event: cancer-related death), OS (event: death for any cause); the log-rank test was used to test for survival differences.

*Results*

Out of 102 patients treated with SABR for lung metastases between October 2003 and October 2011, we selected 67 patients for a total of 90 lesions treated with single fraction SABR. Median follow up time was 24 months. Fifty-six metastases were treated with 3D-CRT, and 34 with Volumetric Modulated Arc Therapy (VMAT).

A single metastatic nodule was treated in 46 patients, 2 nodules in 19 patients and 3 in 2 patients. Primary tumor was NSCLC in 25/67 patients (37.3%), colorectal cancer in 27/67 patients (40.3%) and a variety of other origins in 15 patients (22.4%). Mean age of patients with >1 nodule was inferior (67 vs. 70 years old), the number of patients receiving chemotherapy was higher (28.6% vs. 23.9%), the primary histology was more frequently colorectal cancer (52.4%) and the median follow up was shorter (21 vs. 26 months).

Median disease-free interval (from diagnosis of primary tumor to SABR for lung metastases) was 26 months. Seventeen patients (25.3%) received previous chemotherapy for metastatic disease (58.8% for rectal cancer metastases, 17.6% for melanoma metastases, 11.8% for NSCLC metastases and 11.8 for metastases from other primary), while sixteen patients (23.8%) received other local therapies for metastases prior to SABR (7 thoracic surgery, 5 hepatic surgery and 4 hepatic radiofrequency ablation).

A local failure treated metastasis progression at SABR site was observed in 10 lesions (11.1%), and actuarial LC rates at 1 and 2 years were respectively 93.4% and 88.1% (Figure 1). Seven out of 10 relapses also had a positive FDG-PET scan (in 3 cases, tumor growth or re-growth was documented at contrast CT imaging only).

Systemic failure occurred in 37 patients (55.2%) at a median interval of 8 months after SABR; the crude systemic failure rate did not differ between patients with a single nodule (25/46, 54.3%) and 2-3 metastases (12/21, 57.1%). Progression was only distant in 34 patients and distant/local in 3 patients. Isolated sites of recurrence were lung in 22 patients, liver in 7 patients, brain in 5 patients, bone in 4 patients and adrenal glands in 2 patients; systemic failure occurred in more than one site in 3 patients (adrenal glands and brain, liver and bone, lung and bone). Pattern of failure is shown in Table II.

PFS rates were 72% and 55.4% at 1 and 2 year, respectively (Figure 2).

Twenty-one patients received other treatment at relapse: six patients received a second SABR treatment for lung metastases, six patients received chemotherapy, 2 patients underwent palliative radiotherapy, 1 patient received RF for liver metastases and 5 patients received a combination chemotherapy, palliative radiotherapy, biological agents. At the

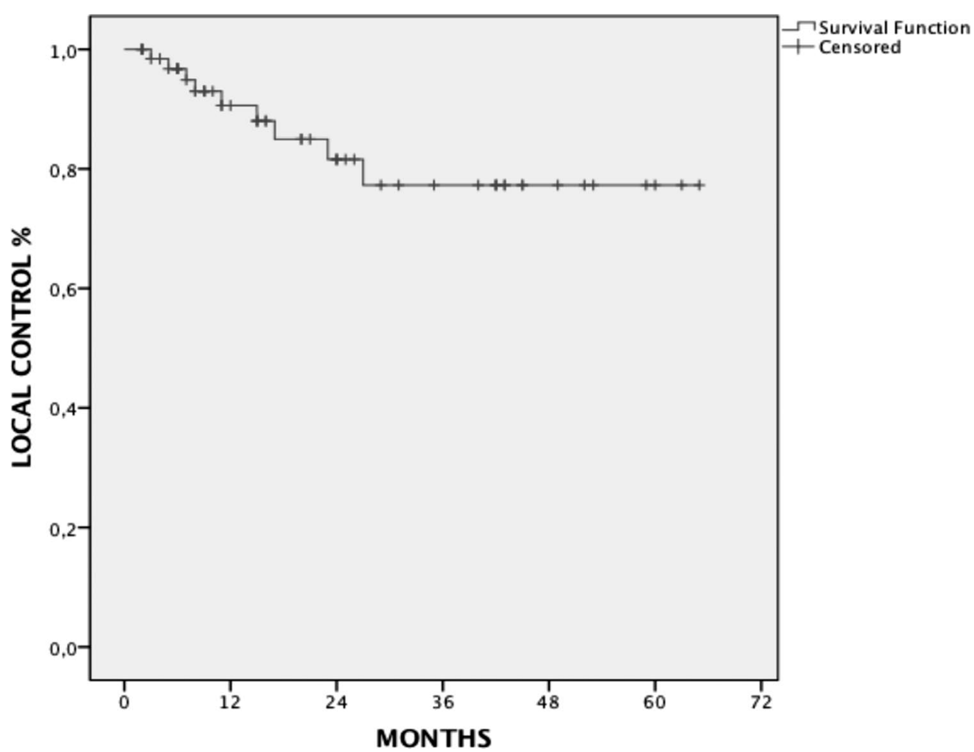


**Figure 1:** Local control.

**Table II**
Pattern of recurrence.

| Recurrence site | Numbers |
|---|---|
| Recurrence at SABR site | 10 |
| Lung | 22 |
| Adrenal gland | 2 |
| Liver | 7 |
| Brain | 5 |
| Bone | 4 |

time of analysis, 25 patients (37.3%) of 67 enrolled have died. At 1 and 2 year, overall survival rates were 85.1% and 70.5%, respectively. CSS rates at 1 and 2 years were 90% and 76% (Figure 3), while OS rates were 85.1% and 70.5%, respectively (Figure 4).

On univariate analysis (Table III), having been treated with other metastasis-directed therapies (surgery, Radiofrequency Ablation) prior to SABR had a detrimental effect on PFS ($p = 0.006$); there was a trend towards a reduced CSS in patients with other untreated controlled metastases ($p = 0.08$). Patients with a disease-free interval longer than 24 months had better CSS (38.7% vs. 16.7%, $p = 0.04$). In patients whose progression occurred in a limited numbers of metastases, amenable to further metastases-directed therapy, a second SABR treatment had a significant positive impact on OS and CSS ($p = 0.03$ and $p = 0.008$, respectively). On multivariate analysis (Table IV), none of these factors was confirmed, even if a disease-free interval longer than 24 months was close to significance for a benefit in CSS ($p = 0.07$; HR 0.34 [95% CI 0.1-1.12]).

Seven cases of grade 1 and 8 cases of RTOG grade 2-3 late radiological toxicity were observed. Six patients experienced a specific toxicity for lesions close to chest wall (rib fracture in 2 case, chronic chest pain in 4 cases). Among the 6 patients who developed chronic chest wall toxicity, 5 were treated with 3D-CRT and 1 with IGRT-VMAT. All patients received a maximum dose to less than 1 cc between 19 and 23 Gy to the chest wall structure (contoured with 2 cm thickness along the cranio-caudal extension of the PTV). Other 4 patients with peripheral lesions close to the chest wall, who did not develop any toxicity, received a maximum dose between 16 and 21 Gy to less than 1 cc, and were treated either with 3D-CRT (1 patients) or with IGRT-VMAT (3 patients).

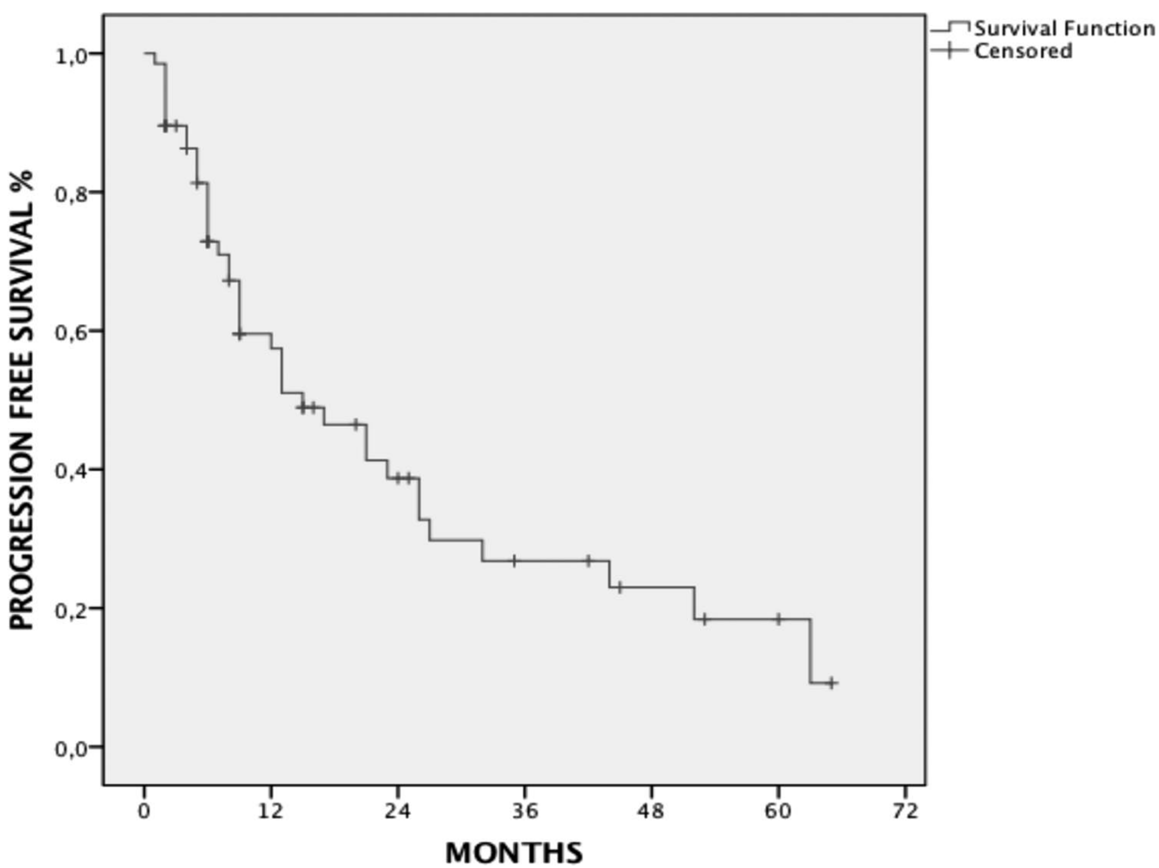


**Figure 2:** Progression-free survival.

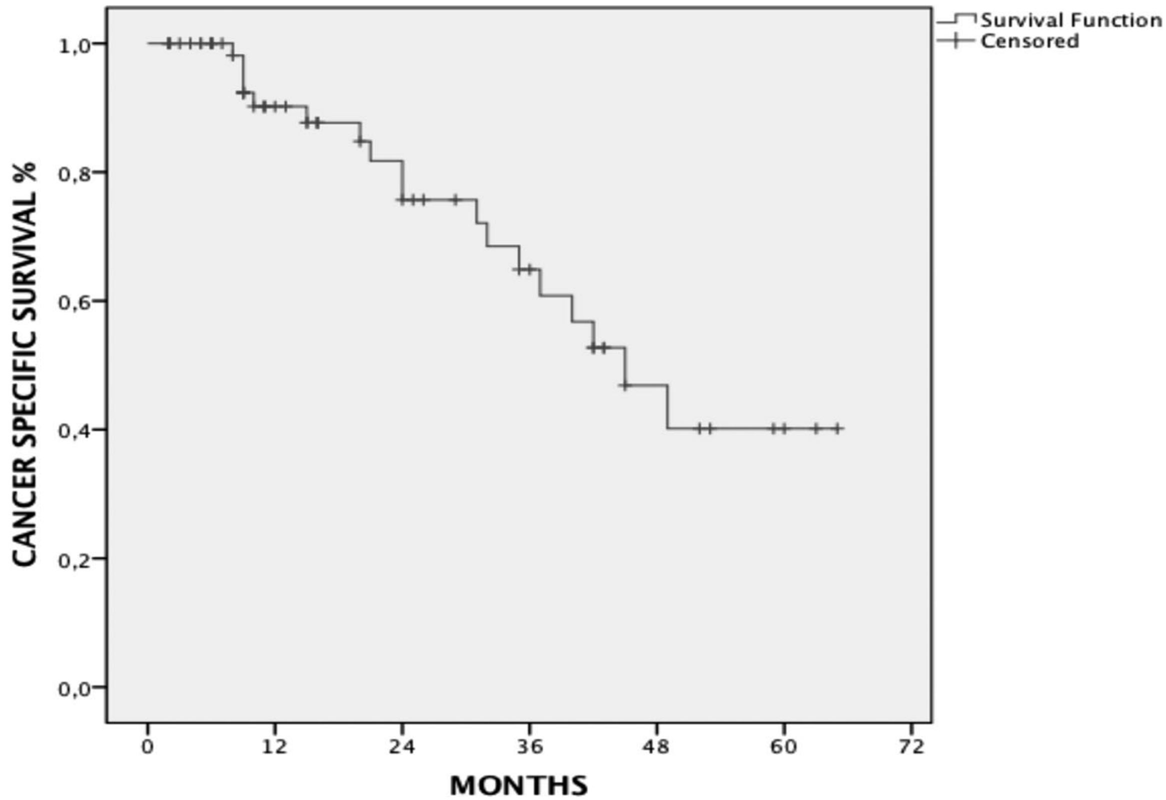


**Figure 3:** Cancer-specific survival.

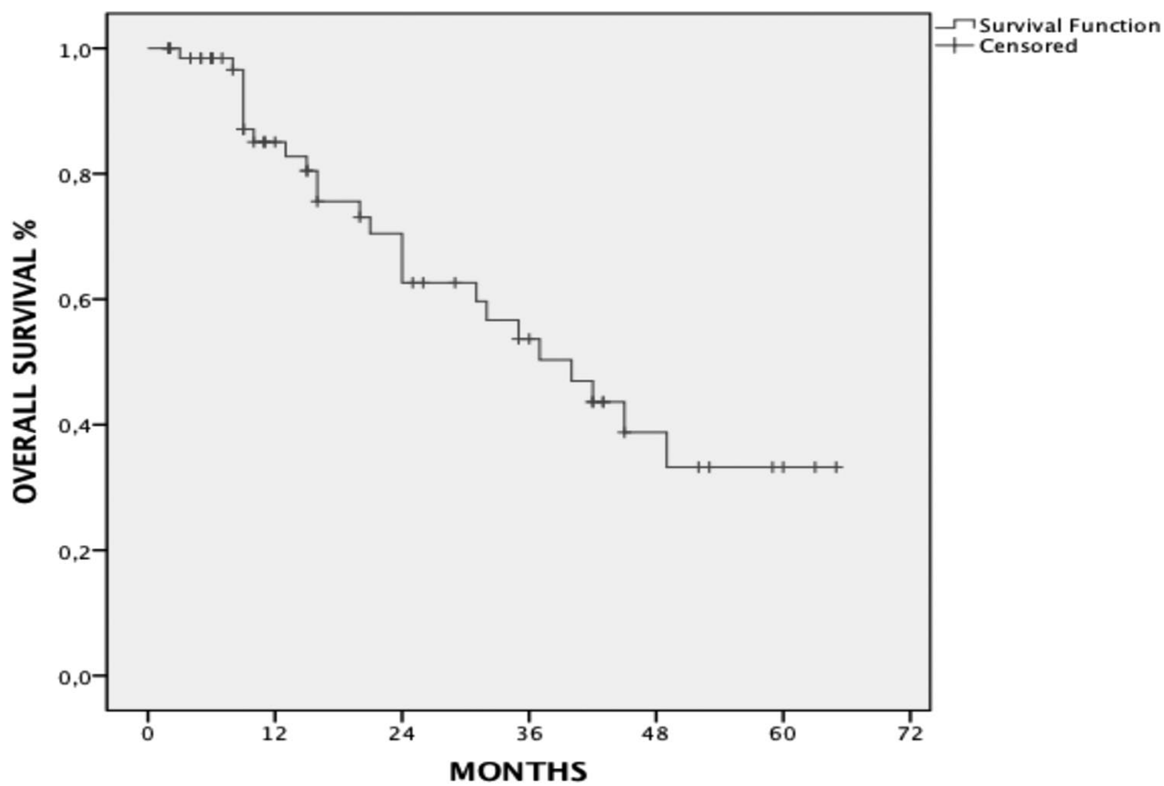


**Figure 4:** Overall survival.

**Table III**
Univariate analysis.

| | OS | | CSS | | LC | | PFS | |
|---|---|---|---|---|---|---|---|---|
| Factors | HR | *p* | HR | *p* | HR | *p* | HR | *p* |
| Age (years) | 1.78 | 0.19 | 1.54 | 0.46 | 1.60 | 0.21 | 1.56 | 0.21 |
| Gender | 1.05 | 0.82 | 1.01 | 0.92 | 1.02 | 0.87 | 1.14 | 0.7 |
| Histology | 1.99 | 0.37 | 0.71 | 0.7 | 1.61 | 0.44 | 1.5 | 0.78 |
| Disease-free interval | 1.53 | 0.47 | 4.16 | 0.04 | 1.00 | 0.95 | 1.06 | 0.81 |
| Other local therapies prior to SABR | 1.37 | 0.54 | 1.20 | 0.65 | 1.05 | 0.31 | 7.6 | 0.006 |
| Other untreated metastasis | 2.5 | 0.11 | 2.9 | 0.08 | 1.39 | 0.53 | 0.53 | 0.47 |
| *n* Lung metastases | 2.45 | 0.29 | 1.3 | 0.52 | 2.31 | 0.31 | 1.13 | 0.94 |
| GTV | 1.03 | 0.85 | 1.04 | 0.83 | 0.82 | 0.36 | 1.01 | 0.90 |
| Other local therapies after SABR | 4.67 | 0.03 | 7.01 | 0.008 | NA | NA | NA | NA |

Abbreviations: OS: Overall Survival; CSS: Cancer-Specific Survival; LC: Local Control; PFS: Progression-free Survival; HR: Hazard Ratio; GTV: Gross Tumor Volume; SABR: Stereotactic Ablative Radiotherapy.

**Table IV**
Multivariate analysis.

| | OS | | CSS | | PFS | |
|---|---|---|---|---|---|---|
| Factors | HR (95% CI) | *p* | HR (95% CI) | *p* | HR (95% CI) | *p* |
| Disease-free interval | NA | NA | 0.3 (0.10-1.1) | 0.07 | NA | NA |
| Other untreated metastasis | 5.7 (0.9-34.7) | 0.07 | 3.6 (0.8-16.4) | 0.09 | 1.2 (2-16.7) | 0.47 |
| Other local therapies prior to SABR | NA | NA | NA | NA | 3.1 (0.8-32.7) | 0.18 |
| Other local therapies after SABR | 1 | 0.99 | 1 | 0.99 | NA | NA |

Abbreviations: OS: Overall Survival; CSS: Cancer-Specific Survival; LC: Local Control; PFS: Progression-free Survival; HR: Hazard Ratio; CI: Confidence Interval; SABR: Stereotactic Ablative Radiotherapy.

## *Discussion*

There are several publications on the efficacy of SABR as an alternative to surgery for patients affected with 1 to 5 lung metastases, a condition that is currently defined as “oligo-metastatic” disease, probably a specific status between locally advanced and widespread metastatic diffusion (2, 3). Aim of the present study was to analyse the clinical outcome of a subgroup of patients who have been treated with single fraction SABR, an ablative strategy that has been investigated by few researchers in this setting and that is similar to the commonly used brain metastases radiosurgery schedule. Metastatic patients usually present with small pulmonary nodules, being diagnosed during regular radiological follow-up, with an increasing proportion of patients showing more than one visible lesions at diagnosis. These specific patients and disease characteristics suggest that probably a single fraction radio-surgical approach would be of value in this subgroup, and we therefore investigated this option. Moreover, advantages related to the high patients compliance, lower costs and high feasibility were taken into account. Previous experiences on single fraction SABR showed promising results in terms of local control and progression-free survival (9,11,12), underlining the prognostic impact of radiation dose (<26 Gy or ≥26 Gy), of the number of treated nodules (single vs. multiple metastases) and of tumours’ dimension (a trend for a lower local control for larger lesions) (11). It has to be noted that in these pioneering experiences various dose levels were tested and the follow-up was limited. The cohort we analysed is homogeneous for clinical parameters and delivered dose, with a difference in the planning and delivery process secondary to the introduction of 4D-CT, IGRT and VMAT in the last years, without any impact on the biologically equivalent dose delivered to tumours. Actuarial local control rates obtained in the present study, 93.4% at 1 year and 88% at 2 years, are well comparable to fractionated SABR results, and modestly superior to the outcomes achieved in other studies on single fraction SABR, perhaps as a consequence of the average higher doses administered in the present study (all patients treated with 26 Gy at 80% isodose). In a recent review by Alongi *et al.* (4), LC rate for fractionated SABR at 2-3 years was in the range 70-90%, with various treatment schedules. As for local control, survival projections are comparable to published experiences on fractionated SABR. In the review by Siva *et al.* (5), the 2-year weighted OS estimation from the largest studies was 54.5%, ranging from higher rates in selected series, such as the study by Norihisa *et al.* (10), reporting an OS rate at 2 years of up to 84%, to lower rates (39%) in the multi-institutional trial conducted by Rusthoven *et al.* (8). Median reported survival times are variable, ranging from 11 months up to more than 40 months (4, 5): In the present study, we obtained a prolonged median survival time (40 months), with a median progression-free survival time of 18 months, in a cohort were single metastases account for 68.7% of treated lesions, 2 metastases for 28.3% and more than 3 metastases for 3% (Table I), with 77.7% of lesions from primary NSCLC and colorectal cancer. Moreover, most patients progressed as truly "oligometastatic" disease, as out of the 34 patients progressing in a destination organ alone after SABR (lung, brain, liver or bone), 15 (44%) had single lesions. The relatively small percentage of patients who received systemic therapy at the time of SABR (25.3%) in our series might be a consequence of the significant proportion of patients with comorbidities, a typical characteristic of a SABR series if compared to surgical registries, and of the high number of single metastatic lesions, a clinical scenario in which the indication to chemotherapy and/or targeted agents is not well defined. The lack of an expected negative impact of the number of lesions on CSS and PFS can be partially explained by a better staging pre-SABR (mandatory CT-PET) and by differences between the 2 groups such as the shorter follow-up time, the lower mean age, the prevalence of colorectal cancer, and the more extensive use of chemotherapy and/or targeted agents in the cohort of patients with multiple nodules. Other factors expected to have a negative impact on PFS and CSS, such as a shorter disease-free interval, a previous metastasis-directed treatment (related to the disease-free interval, as in 16 patients SABR represented a second treatment after a prior failure) or a previous systemic treatment, were selected by univariate analysis but not confirmed on multivariate analysis (probably as a consequence of the limited number of patients included).

Acute and chronic pulmonary toxicity appear comparable to fractionated SABR, and globally very low. In the systematic review by Siva *et al.* (5), there was a 2.6% rate of grade 3 or higher pulmonary toxicity in the single fraction/radiosurgery series, and a 4% rate of grade 3 or higher pulmonary toxicity in the hypo-fractionated radiotherapy series. Higher toxicities were reported when treating centrally located lesions, not eligible to single fraction SABR in our study.

The toxicity of single fraction SABR on chest wall, with 8.9% of rib fractures and chronic pain, appears higher than after fractionated treatments; it has to be noted that initially we did not take into account the dose to the chest wall as a constraint for planning, and that most patients who developed toxicity were treated with 3D-CRT (with higher maximum doses if compared to IGRT-VMAT, mainly because of larger margins around GTV). As a consequence, we currently avoid the use of single fraction SABR in these localizations, preferring a fractionated schedule with similar biologically equivalent dose.

Regarding treatment time, the duration of a single session was approximately 30 minutes for 3D-CRT technique with orthogonal portal imaging verification, and is currently 15-20 minutes with CBCT image guidance and VMAT delivery technique. These treatment times appear acceptable and in none of the patients the treatment was interrupted.

In conclusion, single fraction SABR appears able to obtain satisfactory local control and survival outcomes, playing a significant role in controlling local disease and delaying systemic progression. The feasibility and tolerability of the whole procedure are very high, making this treatment option attractive for patients with single or multiple ≤5 pulmonary nodules.

### *Conflict of Interest*

The authors disclose any conflict of interest with the material included in the study.

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