Supplementary Table S1. Studies on ultracentral lung tumors treated with stereotactic body radiaiton therapy (SBRT) or hypofractionated schedules.

Reference	n	Patients Included	Dose	# Fx	Freq	Platform used	Breath-induced motion Assesment	Motion Assesment	Planning simulation imaging slice thickness	Target definition	Daily positioning and setup	RT technique	Outcomes	Toxicity
Song et al. 2009 [1] -R-	9	NSCLC (Early-stage)	40 - 60	3 - 4	D	NR	Active breathing control Abdominal compression RPM system (gating)	4DCT	NR	GTV + (5 mm laterally and 10 mm longitudinally) = PTV	CBCT Fluoroscopy	IMRT	OS2y 50% LC2y 84.9%	G3+ 33% Bronchial stricture (partial or complete) in 8 patients.
Unger et al. 2010 [2] -R-	20	Primary Metastatic	30-40	5	NR	CyberKnife	Synchrony Respiratory Motion Tracking System	BH	1.25-mm	GTV = PTV	NR	Robotic	OS1y 54% LC1y 63%	G2 esophagitis 1 patient G3 pneumonitis 1 patient G5 fistula (1 patient)
Chaudhuri et al. 2015 [3] -R-	7	Primary Metastatic	50	4 / 5	D	Trilogy TrueBeam CyberKnife	NR	4DCT	NR	ITV + 5 mm = PTV	kV X-ray CBCT	IMRT Robotic	OS2y 80% Primary NSCLC LC2-y 100%	No G2+ toxicity
Haseltine et al. 2016 [4] -R-	18	Primary Metastatic	45 / 50	5	EoD	NR	NR	4DCT	NR	GTV + motion = ITV ITV + 2-3 mm = CTV CTV + 5 mm = PTV	NR	IMRT	Overall (including non ultracentral) OSy 63.9% LC2y 77.4%	G5 toxicity 22.2% (4)
Lischalk et al. 2016 [5] -R-	20	Metastatic	35 - 40	5	D	CyberKnife	Synchrony Respiratory Motion Tracking System	NR	NR	GTV + 5 mm = PTV	NR	Robotic	LC1y 70% OS1y 75%	acute G2+ 1 patient (esophagitis) late G2+ 30% (G2 [atelectasias 3, bronchitis 1], G3 [pneumonitis 1], G4 [atelectasia 1])
Tekatli et al. 2016 [6] -R-	47	NSCLC (primary and recurrent)	60	12	4/week	NR	NR	4DCT	NR	NR	CBCT	VMAT	mOS 15.9m; eOS2y 20.1%	G3+ 38% (G3: pneumonitis 11%, dyspnea 6%, hemoptysis 4% and chest wall pain 4%; G4: hemoptysis 2%; G5: hemorrhage 13%, respiratory failure 2%, others 2%).
Chang et al. 2018 [7] -R-	46	Primary Metastatic	NR	5	EoD	Synergy	NR	4DCT	NR	GTV on 0% (peak inspiratory) GTV 50% (peak expiratory) GTV max intensity projection ITV= sum of GTV's	CBCT	IMRT VMAT	OS2y 50.4%	2y-G3+ 8.7%

										ITV + 5 mm = PTV				
Raman et al. 2018 [8] -R-	16	Primary Metastatic	48 - 60	3 - 10	D/EoD	NR	Abdominal compression	4DCT	NR	GTV = CTV ITV + 5 mm = PTV	CBCT	IMRT VMAT	mOS 23.8m (non metastatic) LC2y 100%	G2+ 7.9% No G4+
Korzets ceder et al. 2018 [9] -R-	20	Primary Metastatic	NR	NR	NR	TrueBeam	NR	4DCT	NR	ITV + 3-4 mm = PTV	CBCT	IMRT VMAT	Not specified for ultracentral	G5 1 patient No other toxicity reported
Lenglet et al. 2019 [10] -R-	77	Primary (early and advanced)	40 - 60	3 - 8	NR	CyberKnife TrueBeam Tomotherapy	Tracking Abdominal compresion (for lower lobes)	4DCT	3-mm	GTV/ITV + 5 mm = PTV	NR	Robotic VMAT	mOS 24m, mPFS 18m, LC18m	G3+ 7.8% (3 pneumonitis, 2 myocardial infarction amd 1 bronchial stricture)
Cong et al. 2019 [11] -R-	51	NSCLC (locally advanced)	35	5	D	CyberKnife	Tracking	4DCT	3-mm	ITV + 3 mm = PTV	NR	IMRT	local recurrence 47.1%	G5 3.9% (2 patients)
Nguyen et al. 2019 [12] -R-	14	Early-stage NSCLC (13) Oligometastatic (1)	40 / 50 / 56 / 60	5 / 5 / 8 / 8	NR	Synergy	Abdominal compression	4DCT	2-mm	GTV + motion = ITV ITV + 5 mm = PTV	CBCT Fluoroscopy	NR	LC2y 89% eOS2y 76%, eOS5y 33%	G2+2y 57.6%
Park et al. 2019 [13] -R-	8	Primary (NSCLC, 3) Consolidative (SCLC, 1) Recurrence (4)	50 - 60	10	NR	NR	Gating (RPM system) Compression belt	4DCT	2-mm 3-mm	GTV = CTV CTV + 5-7 mm = PTV	NR	NR	Respose rate 87.5% Disease control rate 100%	G2 esophagitis (1) No G3+ reported
Meng et al. 2019 [14] -R-	37	Early-stage NSCLC	48 - 60	5 - 10	D	CyberKnife	Synchrony tracking system Xsight spine-tracking system	4DCT	NR	ITV + 5 mm (for Xsight spine and variable dependin fiducial motion) = PTV	NR	Robotic	OS3y 68.7%; OS5y 57.4% PFS3y 47.7%; PFS5y 35.2%	No G3+ toxicity
Henke et al. 2019 [15] -P, phase 1-	5	Primary Metastatic	50	5	NR	MRIdian	Gating (cine MR)	BH	NR	GTV + 5 mm = PTV	NR	IMRT	OS 1y 60% LC1y 80%	Acute G3 (1 esophageal stricture) Acute G4 (1, heart failure)
Cooke et al. 2020 [16] -R-	22	Oligometastases	60	8	EoD	LINAC	NR	4DCT	2.5-mm	ITV + (3 to 5 mm) = PTV	CBCT	IMRT VMAT	LC1y 94.1% OS1y 84.4%	NO acute G3+ toxicity Acute G2 13.6% (1 dysphagia, 2 radiation pneumonitis)

														Late G2 fatige 4.5% (1 patient)
Wang et al. 2020 [17] -R-	88	Primary Metastatic	45 - 60	5 - 15	EoD	NR	NR	4DCT	NR	ITV + (2-3 mm) = CTV CTV + 5 mm = PTV	CBCT kV Xray	IMRT VMAT	LC1y 87.8%; LC2y 81% OS1y 78.6%; OS2y 64.5%; OS3y 53.1%	G3: 6% for pneumonitis, main bronchi occlusion 1% and tracheobronchial perforation in 1% G4: tracheal necrosis 1% G5: hemoptysis 7%, pneumonitis 1% and respiratory failure 3%
Yang et al. 2020 [18] -R-	21	Primary NSCLC Metastatic NSCLC	60	8	D	TrueBeam Edge	NR	4DCT	NR	ITV + 5 mm = PTV	CBCT	VMAT	mOS 15m mPFS 12m; PFS1y 71.1%; PFS2y 64% LC1y 92.9%; LC2y 92.9%	G2 (4 pneumonitis, 1 esophagitis, 1 myelosuppression) NO G3+
Zhao et al. 2020 [19] -R-	41	Primary Metastatic	60	8	D	NR	Free-breathing	4DCT	NR	ITV + 5 mm = PTV	CBCT kV Xray	3DCRT IMRT VMAT	LC1y 97.8%; LC2y 84.5% OS 29.3%	G3 (1 dyspnea and 1 hemoptysis) No G4+
Breen et al. 2021 [20] -R-	110	Primary NSCLC	48 / 60	4 / 8	D	LINAC	NR	4DCT	2-mm	GTV + motion = iGTV iGTV + 5mm = PTV	CBCT	3DCRT VMAT	OS1y 78%, OS2y 57%, OS5y 32%	G2+ 18% (acute); 27% (late) G5 4%
Farrugia et al. 2021 [21] -R-	43	NSCLC	50-60	5	2/week	NR	Gating, abdominal compression	NR	NR	NR	NR	3DCRT VMAT	Local failure 7%, regional failure 11.6%, distant failure 7% eOS2y 53.3%	Acute G3+ 30.2% G3 9.3% (1 cough, 2 chest wall pain and 1 dysphagia)
Lindberg et al. 2021 [22] -P-	65	Primary Metastatic	56	8	E/1-3d No >4/ week	LINAC	Abdominal compression	4DCT	≤3-mm	GTV = CTV CTV + 5-10 mm = PTV	CBCT	IMRT VMAT	LC2y 83%	G3+ 33.8% (22) G5 15.4% (10; 8 hemorrhage, 1 fistula, 1 penumonitis)
Lodeweges et al. 2021 [23] -R-	72	Primary Metastatic	60	12	4 /week	NR	NR	4DCT	NR	ITV + 3 mm = PTV	CBCT	IMRT VMAT	OS1y 77%; OS2y 52% LC1y 98%; LC2y 85%	G3+ 21% G5 14% (all hemorrhage)
Loi et al. 2021 [24] -R-	109	Oligometastases	45 – 70	5 – 10	D	TrueBeam	NR	4DCT	1.5-mm	ITV + 5 mm = PTV	CBCT	VMAT	LC1y 88%; LC2y 78% DMFS1y 54%; DMFS2y 35% PFS1y 53%; PFS2y 30%	G3+ 5% G5 1 esophagitis

													OS1y 88%; OS2y 55%	
Sidiqi et al. 2021 [25] -R (abstract)-	30	NR	40 – 50	5	NR	NR	NR	NR	NR	NR	NR	NR	LC1y 92.3%, LC2y 82.1% OS1y 89.1%, OS2y 65.7	G3+ 13.3% (2 pneumotinits, 1 pleural effusion, 1 large cavitary lesion) G5 3.3% (1, hemoptysis)
Mihai et al. 2021 [26] -R-	57	Primary Oligometastatic	40 – 60	4 – 10	NR	Trilogy TrueBeam	Gating: RPM system +/- DIBH	4DCT	NR	GTV + motion = ITV ITV/GTV + 5 mm = PTV	CBCT	IMRT	LC2y 92%, LC 3y 88.5%, LC4y 79.8% OS2y 55.1%, OS3y 49.3%, OS4y 41.2%	Acute: G3 3.5% (1 fatigue; 2 pneumonitis) Late: G3 5.4% (1 fatigue, 1 dyspnea, 1 aspiration) G5 14% (5 hemoptisis, 2 pneumonia, 1 COPD exacerbation)
Guillaume et al. 2022 [27] -R-	74	Primary Metastatic	NR	5 – 10	E/2d	CyberKnife Synergy Versa HD	Tracking	4DCT	2-mm	GTV/ITV + 5 mm = PTV	NR	NR	LC1y 96.7% LC2y 87.6% mOS 31m	G3 2.7% (pneumonitis and esophagitis) No G4+
Salvestrini et al. 2022 [28] -R-	126	Primary Metastatic	45 – 60	5 – 7	NR	CyberKnife	NR	NR	NR	GTV + 5 mm = PTV	NR	Robotic	OS1y 75%; OS2y 58%; OS5y 23% PFS1y 63%; PFS2y 41%, PFS5y 15%	Acute G3 1 (dyspnea) Late G3 4% (1 pain, 4 dyspnea)
Wang et al. 2022 [29] -R-	58	Primary Metastatic	56	6 – 8	NR	CyberKnife	Fiducial-tracking system	4DCT	NR	GTV + 5 mm = PTV	NR	Robotic	OS1y 94.7%; OS2y 75.0%; and OS5y 45.0%	G3+ 53.5% G5 1 patient (hemoptysis)
Sandoval et al. 2023 [30] -R-	38	Primary Metastatic	50 – 60	3 – 15	NR	MRIdian	Gating (DIBH) tracking	BH	NR	GTV + 3 mm = PTV	MR	IMRT	LC 94.7%	no G3+ acute toxicity Overall (including C and UC): G3 late toxicity 2 (1 pneumonitis, 1 esophagitis)
Song et al. 2023 [31] -R-	27	NSCLC	56 / 60	7 / 10	D	NR	NR	4DCT	NR	GTV + motion = ITV ITV + 5 mm = PTV	CBCT	IMRT	mOS 52m mPFS 38m	G3+18.5%5 G5 7.4% (1 bronchial obstruction, 1 esophageal perforation)
Regnery et al. 2023 [32] -R-	16	Early NSCLC (4) Oligometastatic (12)	50 - 60	10	D	MRIdian	Gating	BH	NR	GTV + 2 mm = CTV CTV + 3 mm = PTV	MR	IMRT	OS2y 67% PFS2y 37%	G3+ 12.5% (1 esophagitis G3, 1 bronchial bleeding G4)
La Rosa et al. *2023** *-R-*	13	Primary Metastatic	60	15	D	MRIdian	Gating (cine-MR)	4DCT	3-mm	GTV + 5 mm = PTV	MR	IMRT	-	No G3+ acute toxicity

*N=number of patients; "# Fx"= number of fractions; Freq=frequency; RT=radiation therapy; -R-=retrospective; -P-=prospective; D=daily; NR=not reported; EoD=every other day; NSCLC=non-small-cell lung cancer; GTV=gross tumor volume; ITV=internal target volume; CTV=clinical target volume; PTV=[lanning target volume; mm=millimeter; G=grade; 4DCT=four-dimensional computed tomography; CBCT=cone-beam computed tomograph;y kV=kilovoltage; OS=overall survival; LC=local control; PFS=progression-free survival; m=media;n "m"=months; "y"=years; 3DCRT=three-dimensional conformal radiation therapy; IMRT=intensity-modulated radiation therapy; VMAT=volumetric modulated arc therapy; *current study.*

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