서울아산병원
Asan Medical Center

Management of Oligometastatic/ Oligoprogressive Disease

Wonjun Ji

Department of Pulmonary and Critical Care Medicine
Asan Medical Center

Contents

Case 1

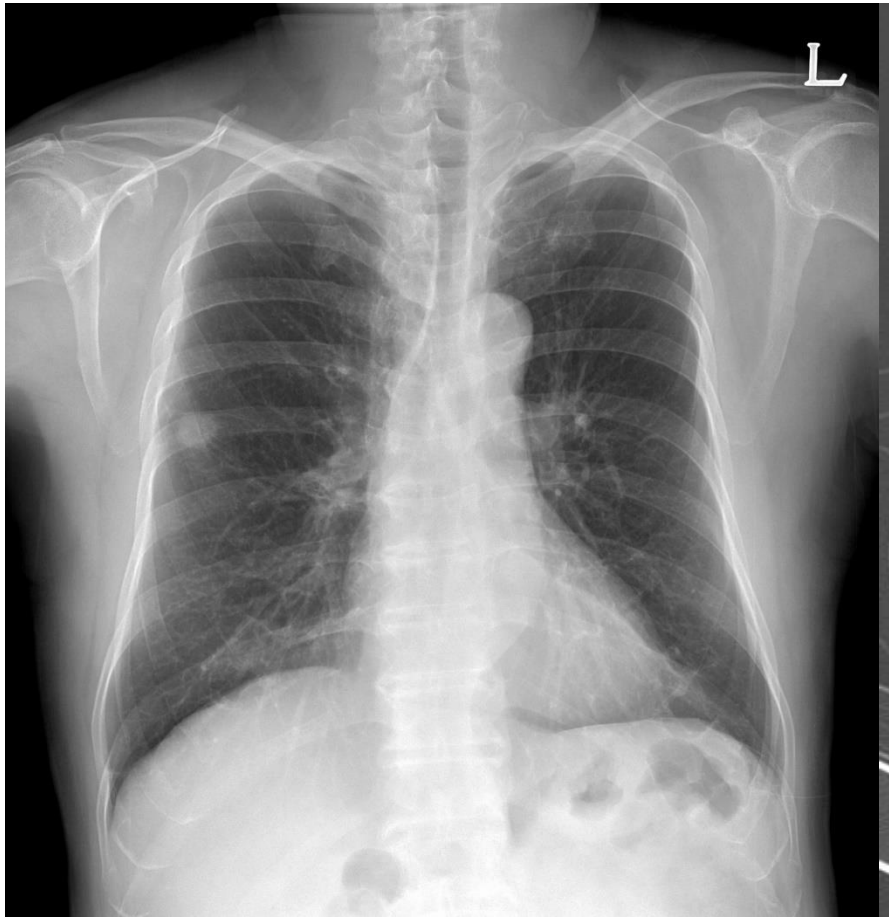
70/M

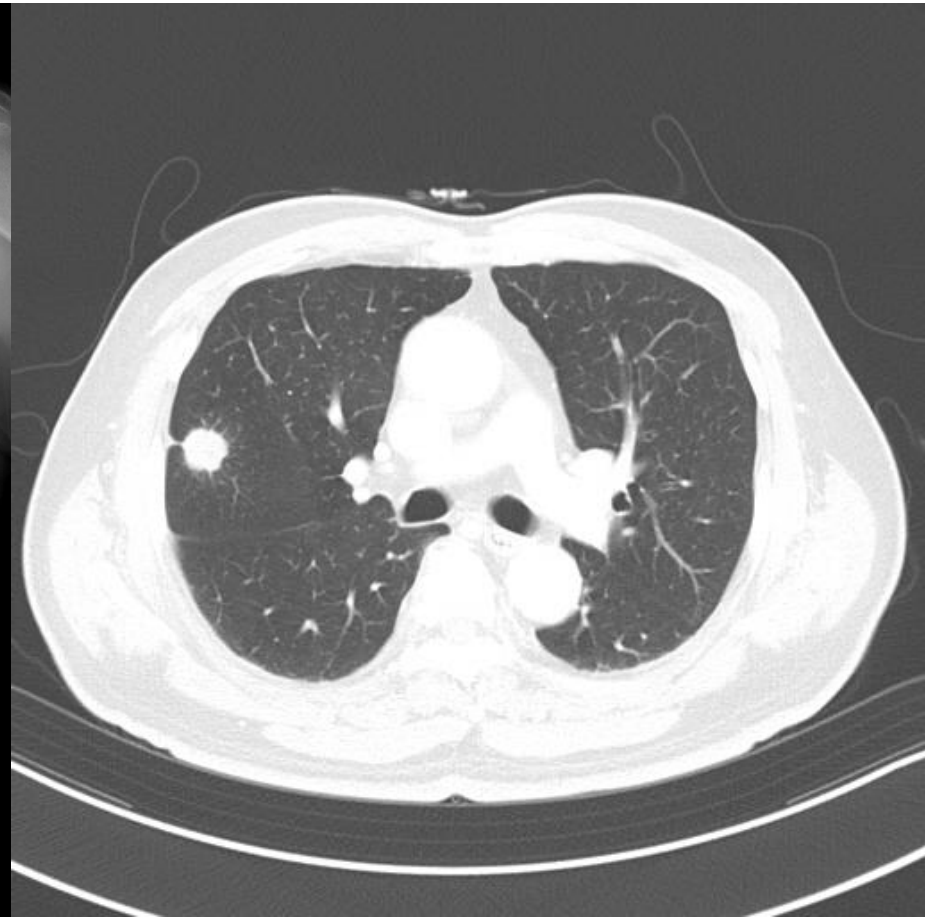
Previous healthy, 20 PY Ex smoker

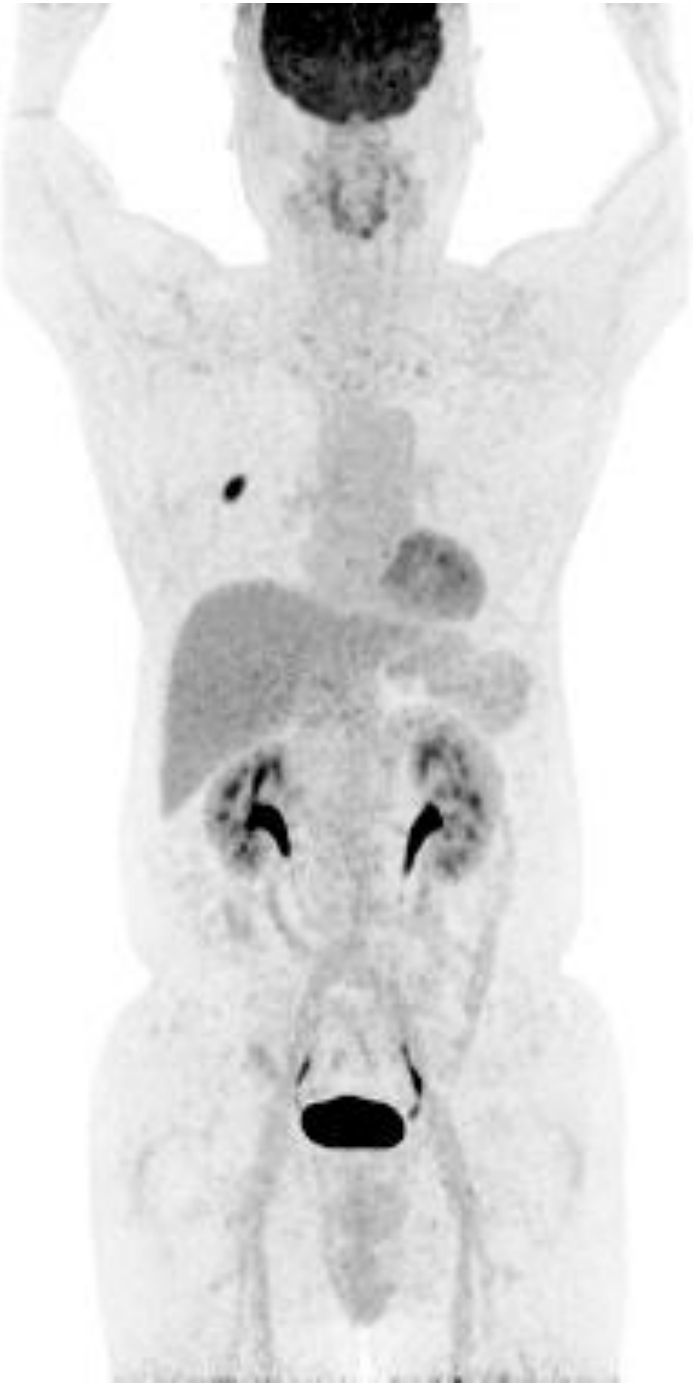
검진 CT상에서 RUL nodule 발견되어 w/u 위해 내원

PFT : FEV1/FVC 65%, FVC 80% (3.53L), FEV1 76%(2.44L), DLco 101%

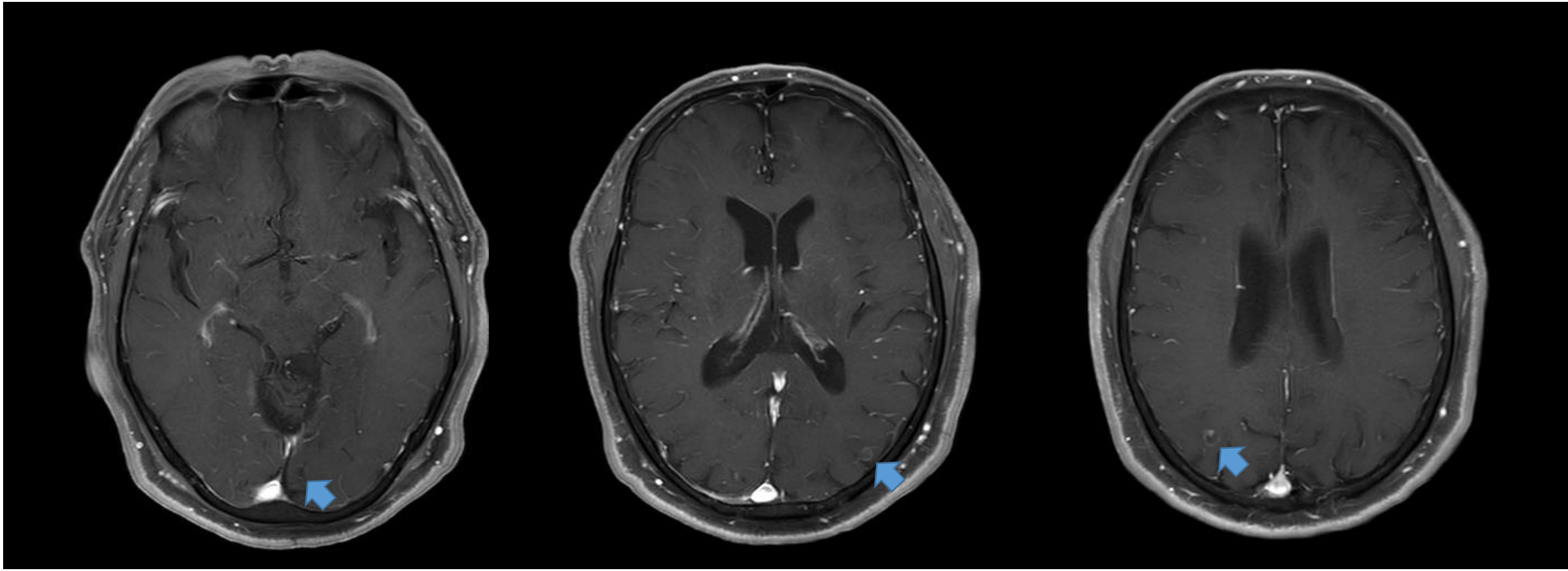
Case 1







Case 1



이 환자의 진단은?

1. Synchronous oligometastasis
2. Metachronous oligometastasis
3. Oligoprogression
4. Oligopersistance

Case 2

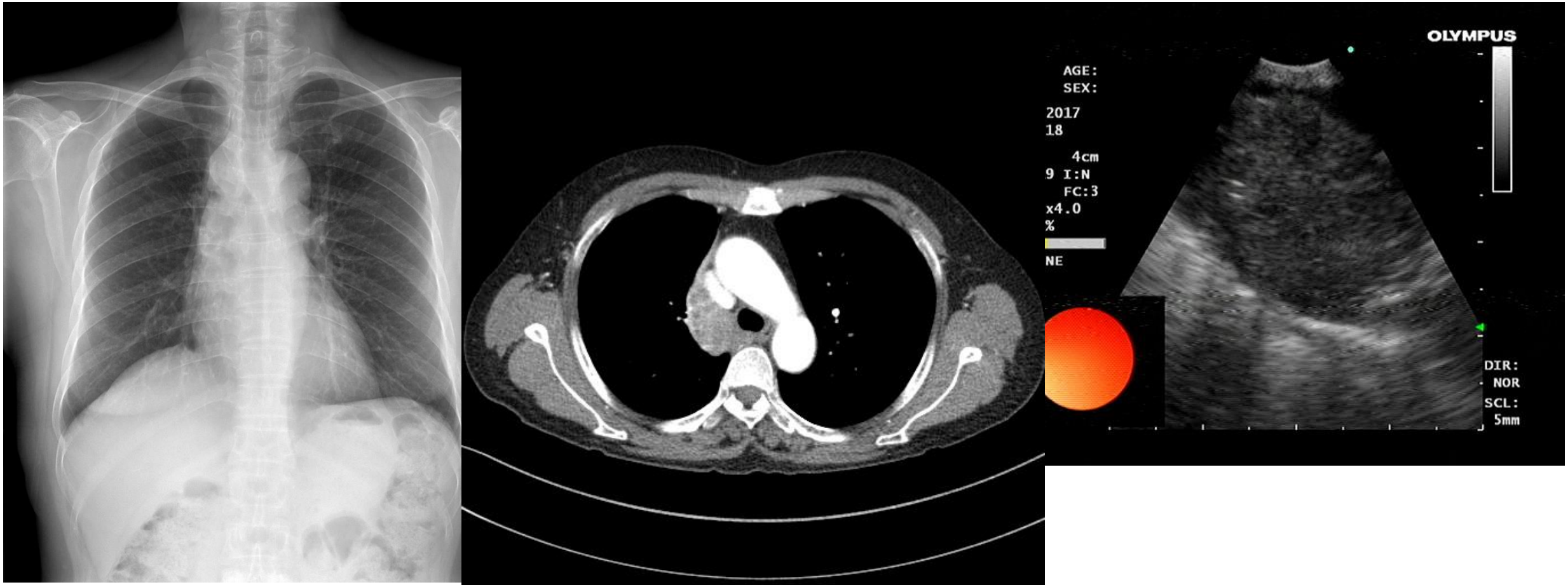
62/F

Never smoker, previous healthy

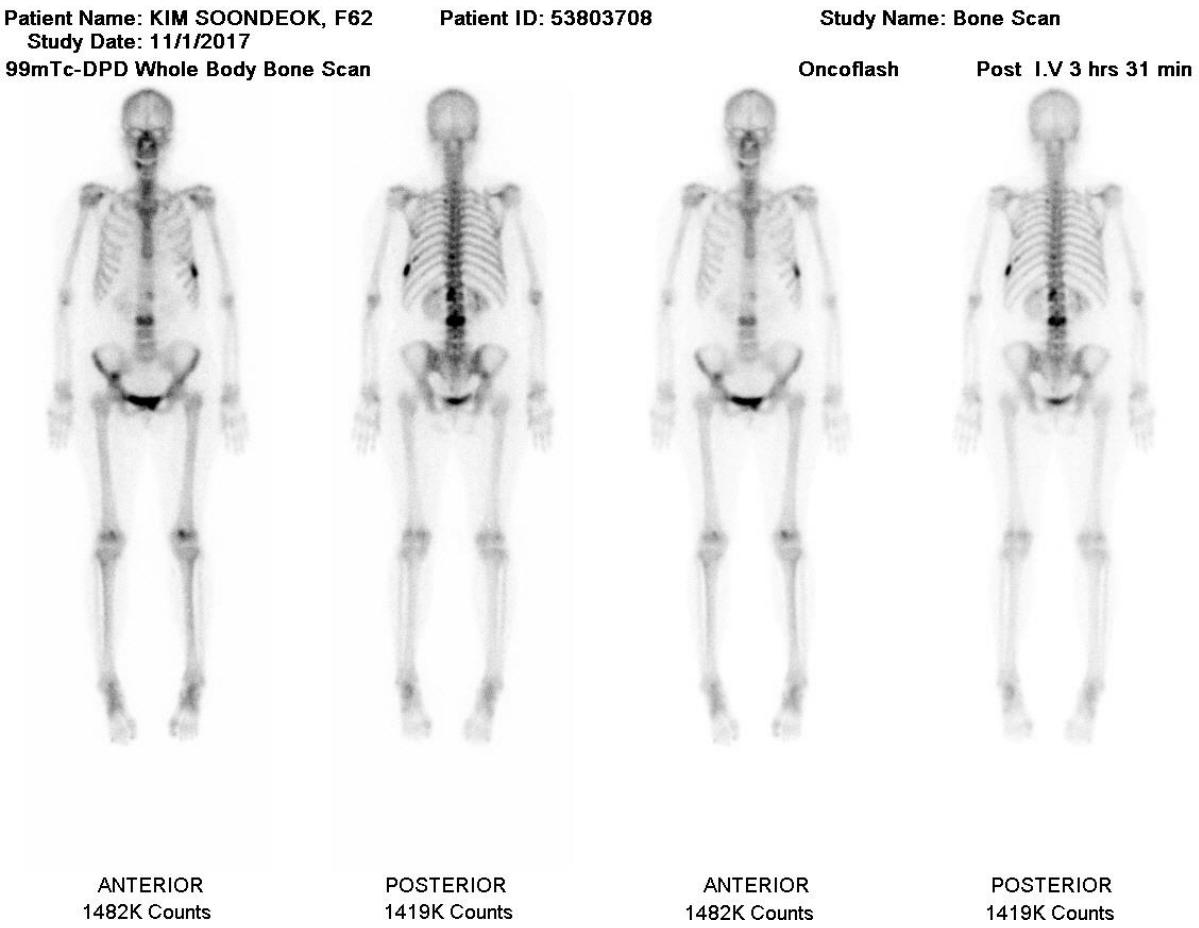
내원 5개월전부터 서서히 발생한, 새벽, 아침에 심해지는 lower back pain 으로 연고지 정형외과 방문

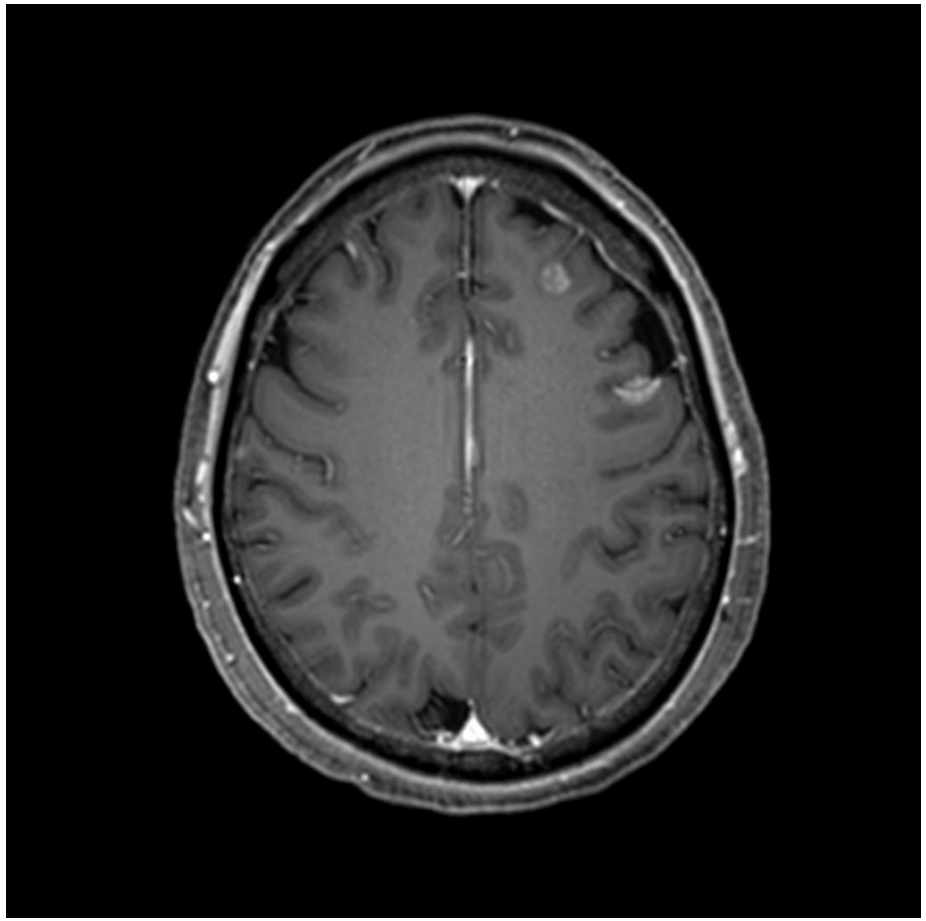
타원 chest CT 상에서 RUL atelectactic mass 와 Bone scan 상에서 multiple bone metastasis 소견으로 w/u 위하여 입원함

Case 2



Case 2


Patient Name: KIM SOONDEOK, F62
Patient ID: 53803708
Study Name: Bone Scan
Study Date: 11/1/2017
99mTc-DPD Whole Body Bone Scan
Oncoflash
Post I.V 3 hrs 31 min
ANTERIOR
1482K Counts
POSTERIOR
1419K Counts
ANTERIOR
1482K Counts
POSTERIOR
1419K Counts

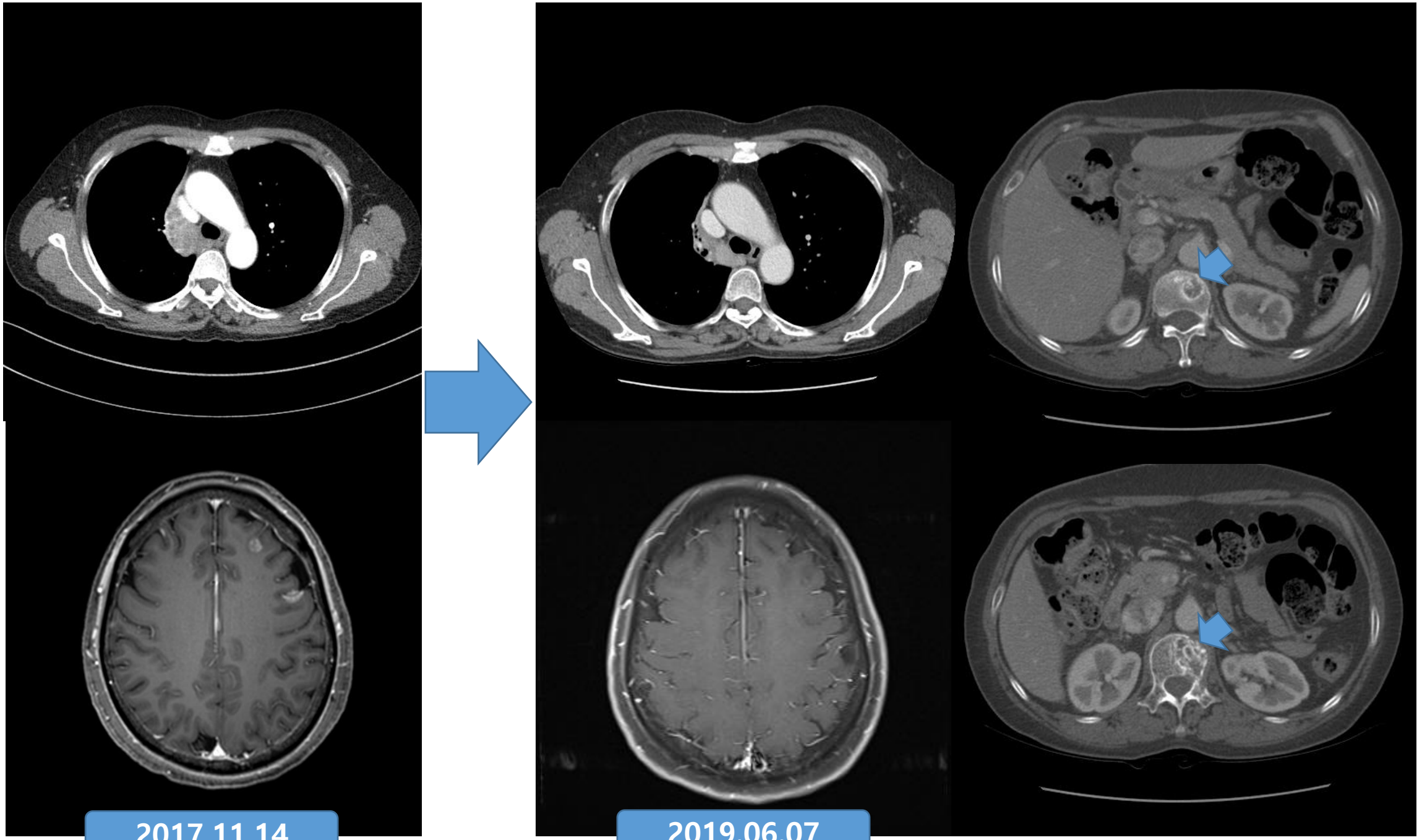


임상경과

NSCLC ACC T4N2M1c brain bone lung

- EGFR 19del+, PD-L1 SP264 10%, 22C3 30%

on Gefitinib 2017.11.14 ➔ PR


2017.11.14
2019.06.07

이 환자의 진단은? 치료는?

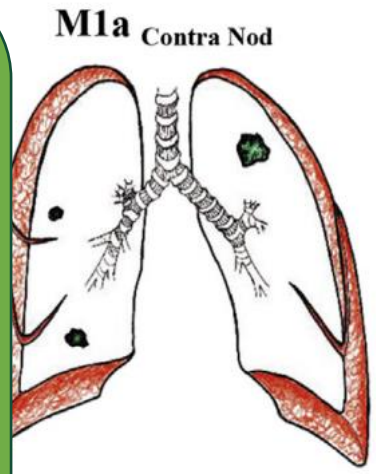
1. Synchronous oligometastasis
2. Metachronous oligometastasis
3. Oligoprogression
4. Oligopersistance

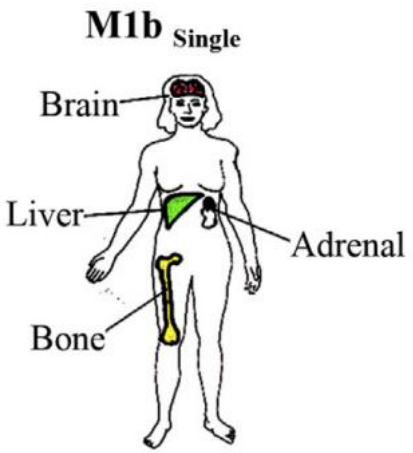
Classification of Oligometastatic NSCLC

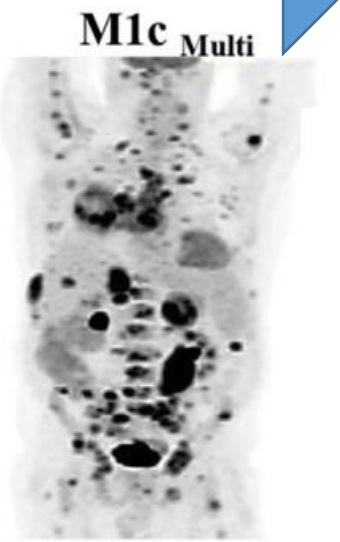
Oligometastatic disease

Local Disease → Oligometastasis → Disseminated disease

1. Potential for modifying the disease course
2. Feasible local treatment with acceptable toxicity
3. Effective systematic therapy
4. Sensitive imaging modality







- *CHEST 2017;151(1);193*
- *Radiother Oncol 2020;148:157*
- *Cancer 2022;14:5339*

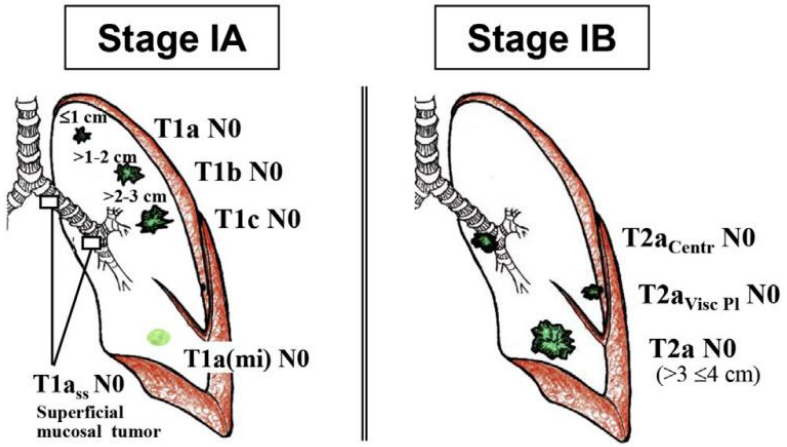
Definition of OMD

Name	Max number of metastasis	Max number of involved organ	Intrathoracic LNs	Pulmonary lesions	Intracranial lesions
EORCT-LCG	5	3	No	Yes	Yes
TNM	1	1	No	Contralateral	Yes
NCCN	3-5	NS	No	Treat as second primary	Yes
ESMO	3	NS	No	Treat as second primary	Yes

- *Cancer 2021;13:4822*

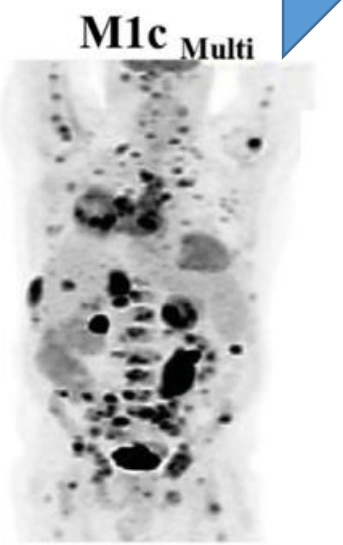
Oligometastatic disease

Local Disease → Oliogometastasis → Disseminated disease



EORTC-LCG definition

1) Number of metastasis site ≤ 5
2) Number of Organ involved ≤ 3
   - Mediastinal LN: Not included
   - Pulmonary Meastasis: Included
   - Intracranial lesion: Included
3) Exclude diffuse serosal metastasis (meningeal, pleural, pericardial and mesenteric)
4) Exclude bone metastasis

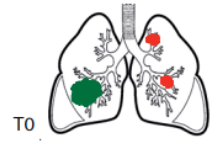


- *CHEST 2017;151(1);193*
- *Radiother Oncol 2020;148:157*
- *Cancer 2022;14:5339*

Classification of OMD

A De-novo oligometastatic disease

Synchronous oligometastatic disease

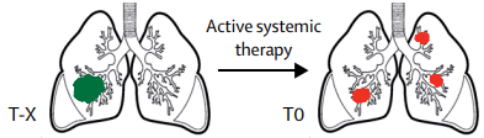


- T0: first time diagnosis of primary cancer (green) and oligometastases (red) within 6 months

Metachronous oligorecurrence

- T-X: diagnosis and treatment of primary cancer (green) in a non-metastatic state
- Systemic therapy-free interval
- T0: First time diagnosis of new oligometastases (red) >6 months after diagnosis of cancer

Metachronous oligoprogression



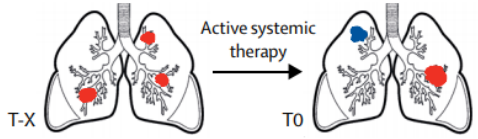
- T-X: diagnosis and treatment of primary cancer (green) in a non-metastatic state
- Under treatment with active systemic therapy
- T0: first time diagnosis of new oligometastases (red) >6 months after diagnosis of cancer

B Repeat oligometastatic disease

Repeat oligorecurrence

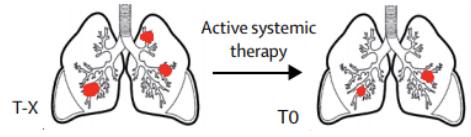
- T-X: diagnosis of oligometastases followed by local treatment or systemic treatment or both
- Systemic therapy-free interval
- T0: diagnosis of new (blue) and growing or regrowing (red) oligometastases

Repeat oligoprogression



- T-X: diagnosis of oligometastases followed by local treatment or systemic treatment or both
- Under treatment with active systemic therapy
- T0: diagnosis of new (blue) and growing or regrowing (red) oligometastases

Repeat oligopersistence



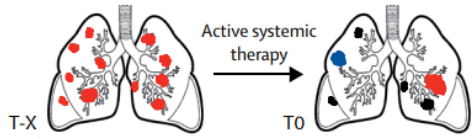
- T-X: diagnosis of oligometastases followed by local treatment or systemic treatment or both
- Under treatment with active systemic therapy
- T0: diagnosis of persistent non-progressive (red) oligometastases

C Induced oligometastatic disease

Induced oligorecurrence

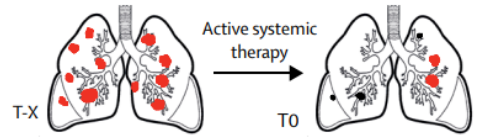
- T-X: diagnosis of polymetastatic metastatic disease followed by systemic treatment with or without local treatment
- Systemic therapy-free interval
- T0: diagnosis of new (blue) and growing or regrowing (red) oligometastases, possible residual non-progressive metastases (black)

Induced oligoprogression



- T-X: diagnosis of polymetastatic metastatic disease followed by systemic treatment with or without local treatment
- Under treatment with active systemic therapy
- T0: diagnosis of new (blue) and growing or regrowing (red) oligometastases, possible residual non-progressive metastases (black)

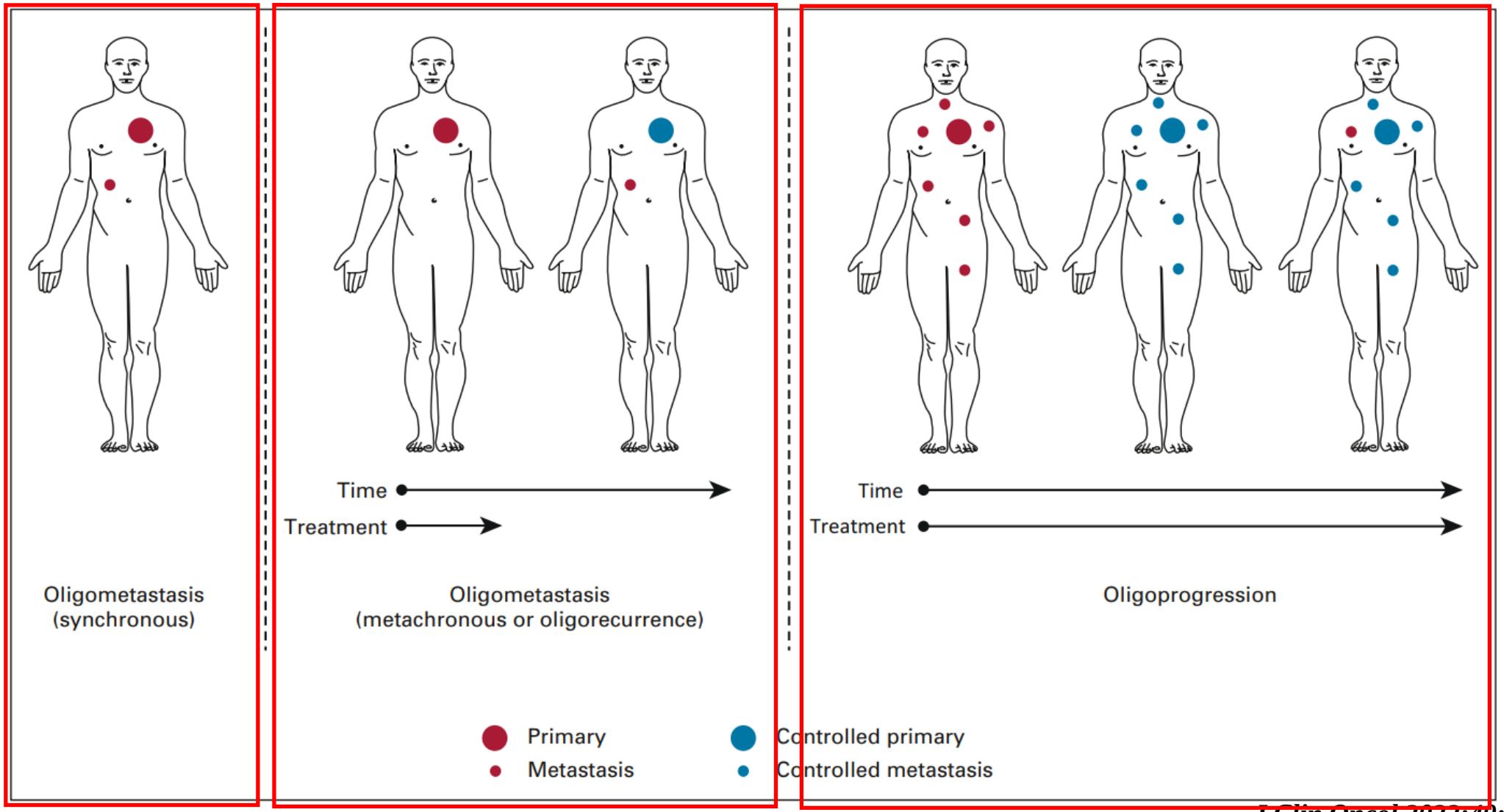
Induced oligopersistence



- T-X: diagnosis of polymetastatic metastatic disease followed by systemic treatment with or without local treatment
- Under treatment with active systemic therapy
- T0: diagnosis of persistent non-progressive oligometastases (red), where response is worse compared with other residual metastases (black)

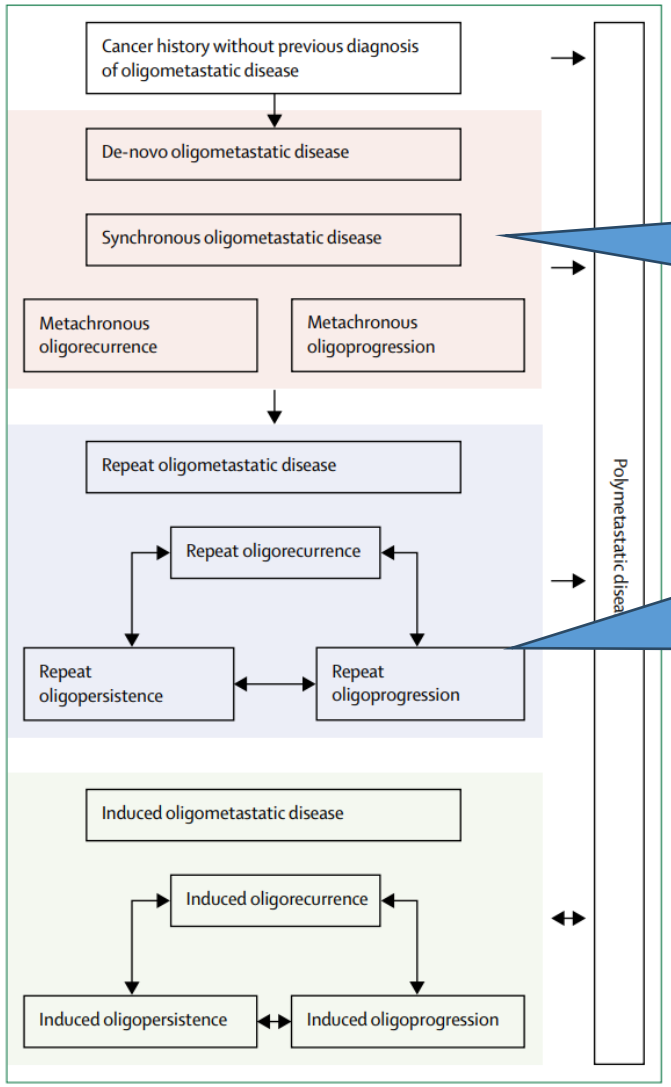
- *Lancet Oncol 2020;21:e18*

Classification of OMD



- *J Clin Oncol 2022;40:635*

Dynamic oligometastatic state model



1. Achieve a status of disesase free status (long term survival)
2. Prolong the time to polymetastatic disease
3. Maintain the patient's quality of life

1. Restore a status of stable disease (long term survival)
2. Restore a status of overall sensitivity to systematic therapy (Eradication of resistance clones)
3. Maintain the patient's quality of life

- *Lancet Oncol 2020;21:e18*
- *J Clin Oncol 2022;40:635*

Clinical Evidences

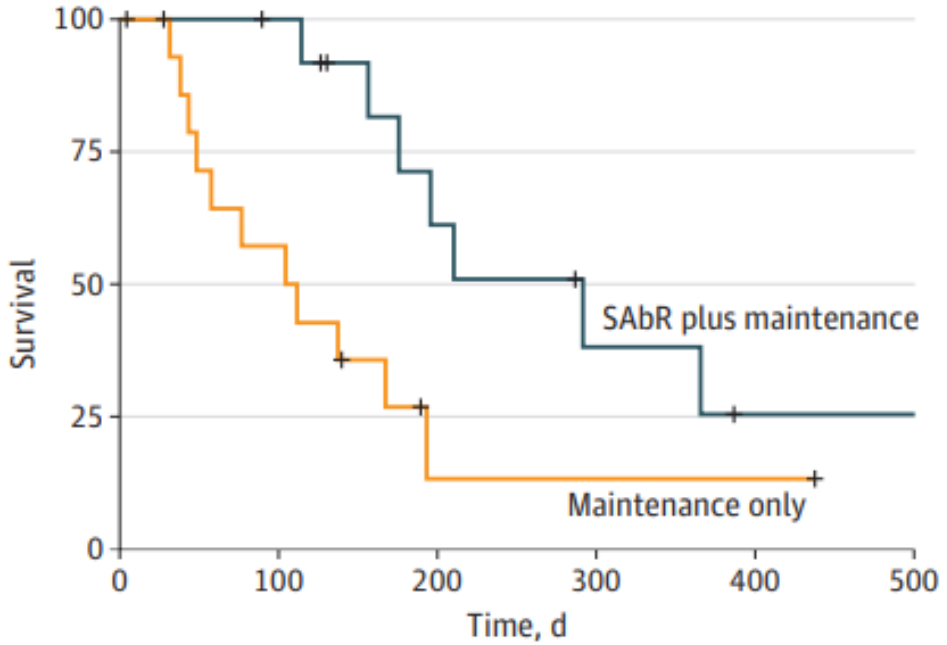
Consolidative Radiotherapy for Limited Metastatic Non-Small-Cell Lung Cancer

A Phase 2 Randomized Clinical Trial

Puneeth Iyengar, MD, PhD; Zabi Wardak, MD; David E. Gerber, MD; Vasu Tumati, MD; Chul Ahn, PhD; Randall S. Hughes, MD; Jonathan E. Dowell, MD; Naga Cheedella, MD; Lucien Nedzi, MD; Kenneth D. Westover, MD, PhD; Suprabha Pulipparacharuvil, PhD; Hak Choy, MD; Robert D. Timmerman, MD

- Prospective phase II RCT
- 29 NSCLC patients (EGFR- ALK-)
- ≤5 synchronous oligometastatic lesions
- More than SD after initial treatment

- Significant PFS: 9.7Mo SABR arm vs 3.5 Mo control (HR 0.304; 95% CI 0.113-0.815, P=0.01)
- Toxicity was similar in both arm



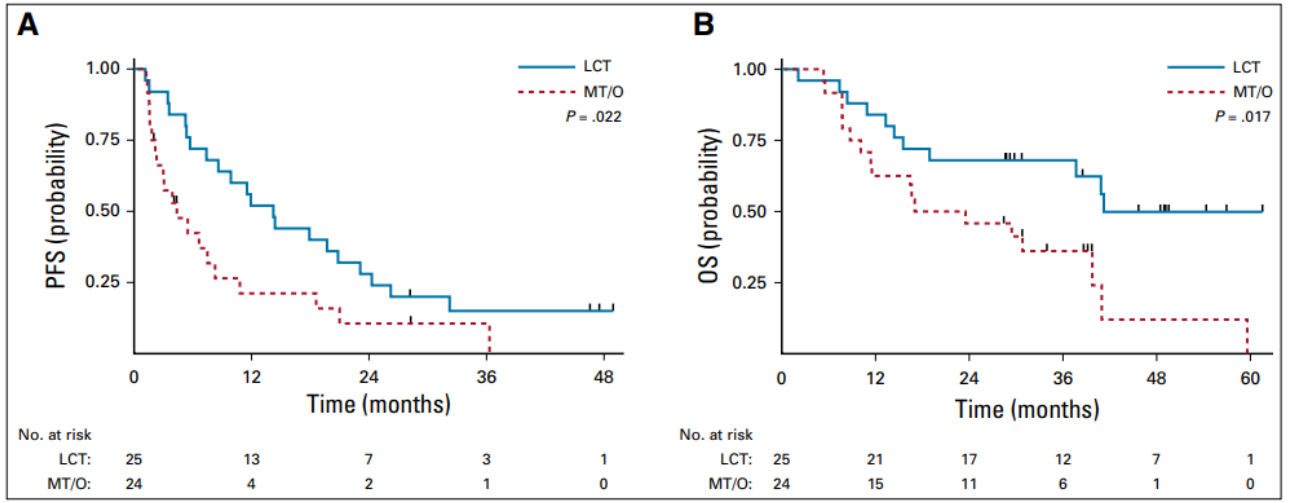
No. at risk

SAbR plus maintenance	14	12	6	3	1
Maintenance only	15	8	1	1	1

- *JAMA Oncol 2018;4(1):e173501*

Local Consolidative Therapy Vs. Maintenance Therapy or Observation for Patients With Oligometastatic Non–Small-Cell Lung Cancer: Long-Term Results of a Multi-Institutional, Phase II, Randomized Study

Daniel R. Gomez, MD[1]; Chad Tang, MD[1]; Jianjun Zhang, MD, PhD[1]; George R. Blumenschein Jr, MD[1]; Mike Hernandez, MS[1]; J. Jack Lee, PhD[1]; Rong Ye, MS[1]; David A. Palma, MD, PhD[2]; Alexander V. Louie, PhD, MSc[2]; D. Ross Camidge, MD, PhD[3]; Robert C. Doebele, MD, PhD[3]; Ferdinandos Skoulidis, MD, PhD[1]; Laurie E. Gaspar, MD[3]; James W. Welsh, MD[1]; Don L. Gibbons, MD[1]; Jose A. Karam, MD[1]; Brian D. Kavanagh, MD, MPH[3]; Anne S. Tsao, MD[1]; Boris Sepesi, MD[1]; Stephen G. Swisher, MD[1]; and John V. Heymach, MD, PhD[1]



- Prospective phase II RCT
- 49 NSCLC patients (3 EGFR+ in both arm, 2 ALK+ in LCT arm)
- ≤3 synchronous oligometastatic lesions
- No progression after initial treatment

- Significant PFS: 14.2 Mo vs 4.4 Mo
- Significant OS: 41.2 Mo vs 17.0 Mo
- Survival after PD: 37.6 Mo vs 9.4 Mo
- Toxicity: ≥ Gr3 20% vs 8%, No Gr 4-5

TABLE 2. Summary of Multivariable Cox Proportional Hazards Model That Includes Treatment Arm, Number of Metastases, and *ALK/EGFR* Alteration

Variable	HR	95% CI	*P*
Treatment			
MO	Ref		
LCT	0.46	(0.21 to 0.99)	.048
No. of metastases			
1	Ref		
2-3	1.50	(0.69 to 3.26)	.310
Mutation status			
None	Ref		
EGFR/EML4ALK	0.15	(0.02 to 1.12)	.065

Abbreviations: HR, hazard ratio; MO, maintenance therapy or observation; Ref, reference; LCT, local consolidative therapy.

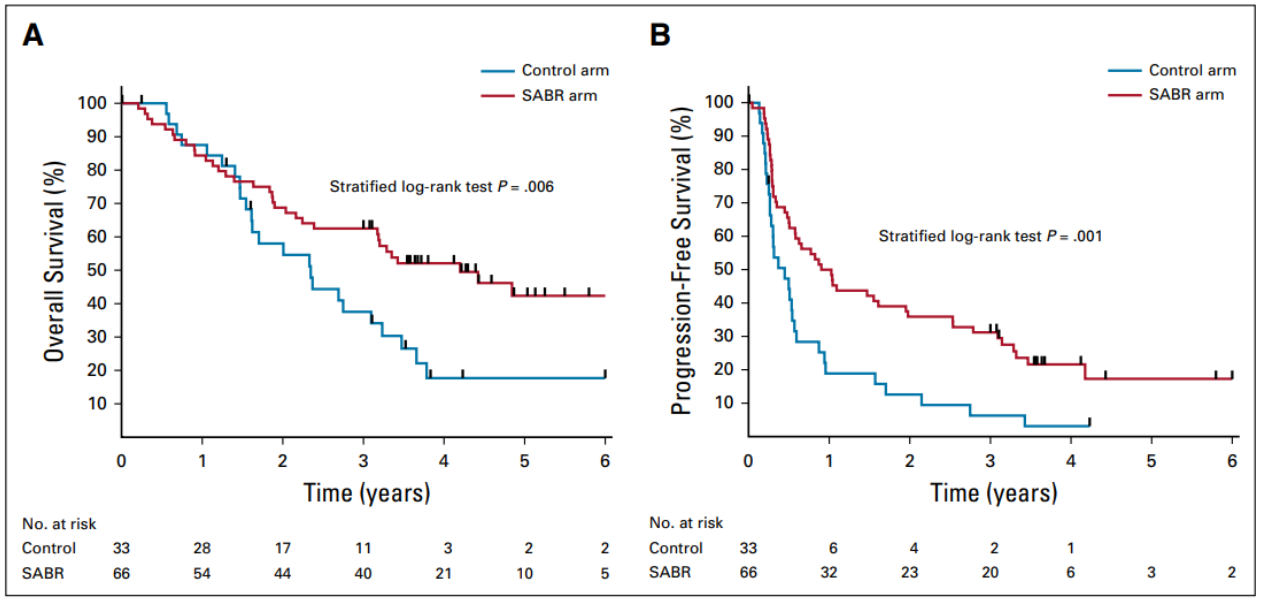
- ***Lancet Oncol 2016;17:1672***
- ***J Clin Oncol 2019;37:1558***

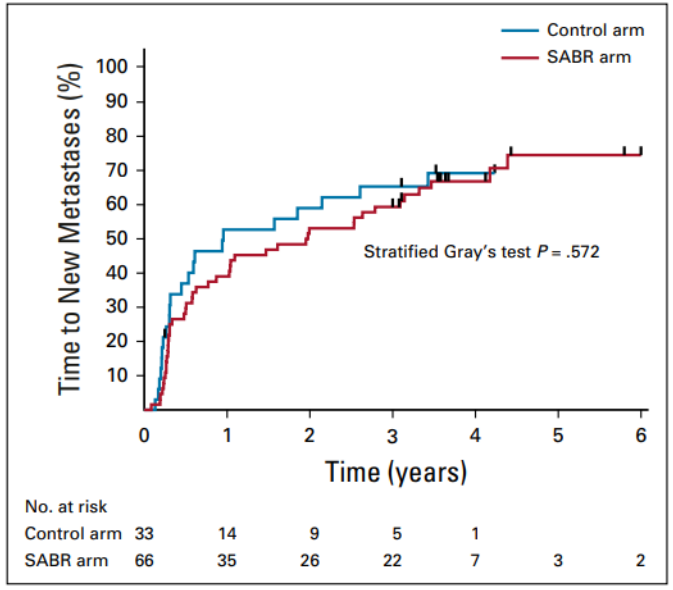
Stereotactic Ablative Radiotherapy for the Comprehensive Treatment of Oligometastatic Cancers: Long-Term Results of the SABR-COMET Phase II Randomized Trial

David A. Palma, MD, PhD[1]; Robert Olson, MD, MSc[2]; Stephen Harrow, MBChB, PhD[3]; Stewart Gaede, PhD[1]; Alexander V. Louie, MD, PhD[4]; Cornelis Haasbeek, MD, PhD[5]; Liam Mulroy, MD[6]; Michael Lock, MD[1]; George B. Rodrigues, MD, PhD[1]; Brian P. Yaremko, MD, PEng[1]; Devin Schellenberg, MD[7]; Belal Ahmad, MD[1]; Sashendra Senthi, MD, PhD[8]; Anand Swaminath, MD[9]; Neil Kopek, MD[10]; Mitchell Liu, MD[11]; Karen Moore, MSc[3]; Suzanne Currie, MSc[3]; Roel Schlijper, MD[2]; Glenn S. Bauman, MD[1]; Joanna Laba, MD[1]; X. Melody Qu, MD, MPH[1]; Andrew Warner, MSc[1]; and Suresh Senan, MBBS, PhD[5]

- Prospective phase II RCT
- 99 multitumor patients, 18 lung cancer
- ≤5 synchronous oligometastatic lesions
- Primary tumor had to be controlled before local treatment (at least 3 Mo)
- SOC+SABR vs SOC 2:1 ratio

- Significant PFS: 17.3% (5yrs) vs 3.2%(4yrs)
- Significant 5yrs OS: 42.3% vs 17.7%
- Toxicity ≥ Gr2 29% vs 9%, No Gr 3-5





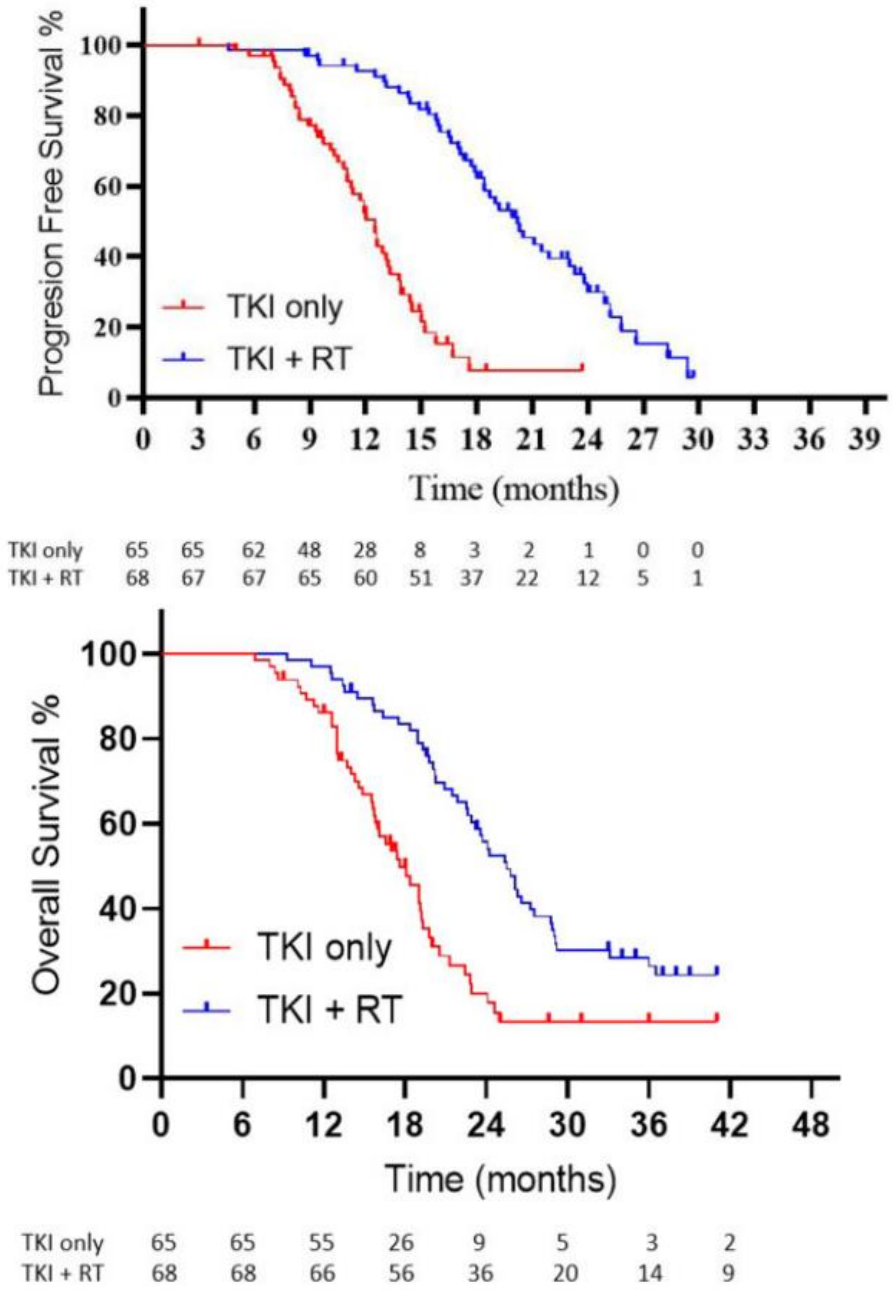
- *Lancet 2017;393:2051*
- *J Clin Oncol 2020;38:2830*

Randomized Trial of First-Line Tyrosine Kinase Inhibitor With or Without Radiotherapy for Synchronous Oligometastatic *EGFR*-Mutated Non-Small Cell Lung Cancer

Xiao-Shan Wang, MD,[1,‡] Yi-Feng Bai, MD,[1,‡] Vivek Verma, MD,[2] Rui-Lian Yu, MD,[1] Wei Tian, MS,[1] Rui Ao, MD,[1] Ying Deng, MD,[1] Jian-Ling Xia, MD,[1] Xue-Qiang Zhu, MD,[1] Hao Liu, MD,[1] Hai-Xia Pan, MD,[1] Lan Yang, MD,[1] Yang-Ke He, MD,[1] Han-Song Bai, MD,[3] Xing Luo, MD,[3] Yan Guo, MS,[3] Ming-Xiu Zhou, MD,[3] Yue-Mei Sun, MD,[4] Zi-Can Zhang, MD,[4] Si-Min Li, MD,[3,5] Xue Cheng, MD,[3] Bang-Xian Tan, MD,[3] Liang-Fu Han, MD,[6] Ying-Yi Liu, MD,[7] Kai Zhang, MD,[8] Fan-Xin Zeng, PD,[9] Lin Jia, MD,[10] Xin-Bao Hao, MD,[11] You-Yu Wang, MD,[1] Gang Feng, MD,[1] Ke Xie, MD,[1] You Lu, MD,[12] Ming Zeng, MD, PhD[1,*]

- Prospective phase III RCT, SYNDAS trial
- 133 EGFR mutant NSCLC without brain mets
- ≤5 oligometastatic lesions, ≤2 lesion in any one organ
- First-generation TKI: gefitinib, erlotinib, icotinib
- TKI with RT (25-40 Gr/5Frs) vs TKI alone

- Significant PFS: 20.2 Mo vs 12.8 Mo
- Significant mOS: 25.5 Mo vs 17.4 Mo
- Toxicity: ≥ Gr2 9% vs 6%, No Gr 3-5



- *JNCI J Natl Cancer Inst 2022;114(5):djac015*

Randomized Trial of First-Line Tyrosine Kinase Inhibitor With or Without Radiotherapy for Synchronous Oligometastatic *EGFR*-Mutated Non-Small Cell Lung Cancer

Xiao-Shan Wang, MD,[1,‡] Yi-Feng Bai, MD,[1,‡] Vivek Verma, MD,[2] Rui-Lian Yu, MD,[1] Wei Tian, MS,[1] Rui Ao, MD,[1] Ying Deng, MD,[1] Jian-Ling Xia, MD,[1] Xue-Qiang Zhu, MD,[1] Hao Liu, MD,[1] Hai-Xia Pan, MD,[1] Lan Yang, MD,[1] Yang-Ke He, MD,[1] Han-Song Bai, MD,[3] Xing Luo, MD,[3] Yan Guo, MS,[3] Ming-Xiu Zhou, MD,[3] Yue-Mei Sun, MD,[4] Zi-Can Zhang, MD,[4] Si-Min Li, MD,[3,5] Xue Cheng, MD,[3] Bang-Xian Tan, MD,[3] Liang-Fu Han, MD,[6] Ying-Yi Liu, MD,[7] Kai Zhang, MD,[8] Fan-Xin Zeng, PD,[9] Lin Jia, MD,[10] Xin-Bao Hao, MD,[11] You-Yu Wang, MD,[1] Gang Feng, MD,[1] Ke Xie, MD,[1] You Lu, MD,[12] Ming Zeng, MD, PhD[1,*]

Table 2. Multivariable analyses of progression-free and overall survival

	Progression-free survival		Overall survival	
Variable[a]	HR (95% CI)	P[b]	HR (95% CI)	P[b]
Zubrod performance status (0 vs 1-2)	0.50 (0.22 to 0.75)	.02	0.01 (0.01 to 0.44)	.02
Clinical T classification (T3-4 vs T1-2)	1.10 (0.99 to 1.22)	.09	2.06 (1.08 to 5.54)	.02
Clinical N classification (N2-3 vs N0-1)	—	—	1.56 (1.19 to 3.69)	.06
Number of metastases (3-5 vs 1-2)	1.96 (1.30 to 4.70)	.004	1.93 (1.21 to 3.07)	.004
EGFR mutation (exon 19 deletion vs exon 21 mutation)	0.94 (0.61 to 1.43)	.09	0.09 (0.02 to 0.38)	.001
Randomization arm (TKI only vs TKI + RT)	1.39 (1.07 to 1.95)	.005	2.11 (1.31 to 5.97)	.004

[a]Only variables included in the final multivariable model are displayed. The notation in parentheses refers to comparator group vs reference group. — = N/A; CI = confidence interval; *EGFR* = epidermal growth factor receptor; HR = hazard ratio; RT = radiation therapy; TKI = tyrosine kinase inhibitor.
[b]All tests were 2-sided.

- *JNCI J Natl Cancer Inst (2022) 114(5): djac015*

Phase II study of stereotactic radiosurgery for the treatment of patients with oligoprogression on erlotinib

Jared Weiss*, Brian Kavanagh, Allison Deal, Liza Villaruz, James Stevenson, Ross Camidge, Hossein Borghaei, Jack West, Padmini Kirpalani, David Morris, Carrie Lee, Chad V. Pecot, Timothy Zagar, Thomas Stinchcombe, Nathan Pennell

Lineberger Cancer Center at the University of North Carolina, 170 Manning Drive, Room 3115, Campus Box 7305, Chapel Hill, NC 27514, United States

- Prospective single arm phase II trial
- 25 EGFR mutant NSCLC on erlotinib
- ≤3 extra-cranial oligoprogession

- Median PFS: 6 Mo (95% CI 2.5-11.6)
- Median OS: 29 Mo (95% CI 21.7-36.3)
- Toxicity: ≥ Gr3 6% (including pneumonitis)

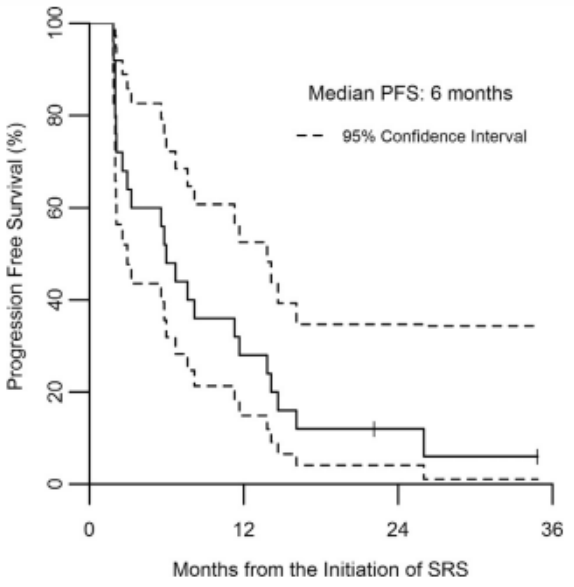


Fig. 1. PFS.

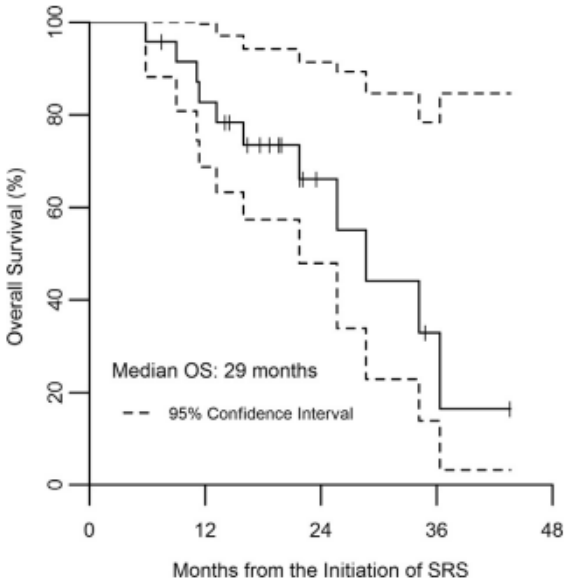


Fig. 2. OS.

- ***Cancer treat res commun 2019;19:100126***

Original Article

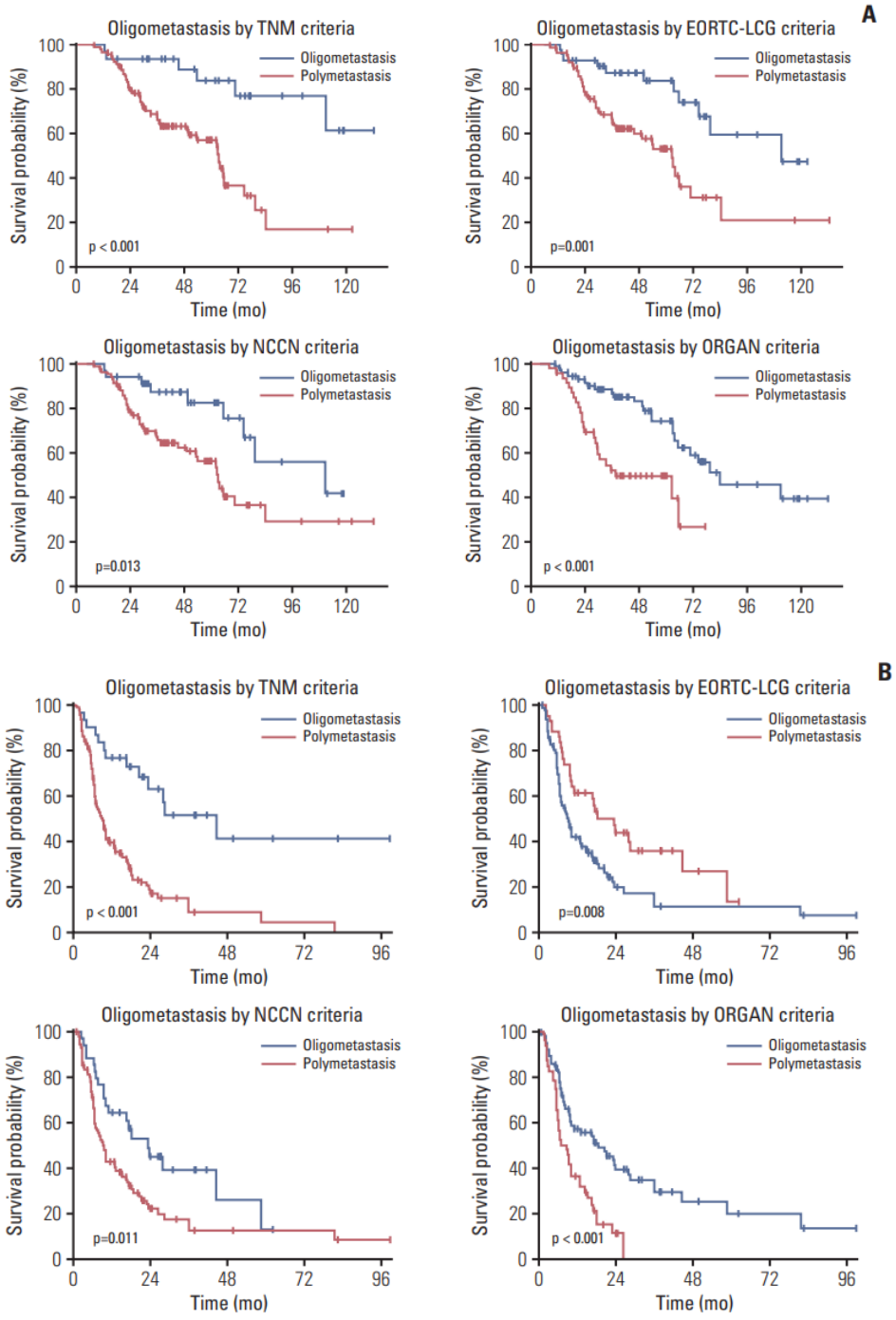
Optimal Definition of Oligometastasis Showing Survival Benefits of Local Therapies during Tyrosine Kinase Inhibitor Treatment

Yoon Jung Jang[1,2], Dong-gon Hyun[3], Wonjun Ji[3], Chang-Min Choi[2,3], Shinkyo Yoon[2], Dae Ho Lee[2], Sang-We Kim[2], Ja

[1]Department of Hematology and Oncology, Korea Cancer Center Hospital, Korea Institute of Radiological and Medical Sciences, Seo
[2]Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, [3]Department of Pulmonary and Cri
Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

- Retrospective single center study
- 117 EGFR or ALK mutant NSCLC (2011-2020)

- Median PFS from LCT to systemic progression : 10.3 Mo (95% CI 5.5-15.1)
- Median PFS from use of TKI to systemic progression : 30.9 Mo (95% CI 5.5-15.1)
- Median OS: 70.8 Mo (95% CI 56.6-85.1)



Ongoing Clinical Trials

Trial Name	Trial Identifier	Histology	Number of Metastasis	Systemic Therapy	Local Therapy	Primary Endpoint
OMEGA	NCT03391869	NSCLC	1-3	Chemo, IO. TKI	LCT	OS
SARON	NCT02417662	NSCLC	1-5	Per physician	RT	OS
NRG LU002	NCT03137771	NSCLC	1-3	chemo, IO	RT	PFS, OS
CORE	NCT02759783	NSCLC, breast, prostate	1-3	Per physician	RT	PFS
OITROLC	NCT02076477	NSCLC	1-5	Chemo	RT	ORR
SABR-COMET-3/10	NCT03862911 NCT03721341	Mixed	1-3 1-10	Per physician	RT	OS
LONESTAR	NCT03391869	NSCLC	1-3 (subset)	Ipilimumab/ Nivolumab	RT	OS
NORTHSTAR	NCT03410043	NSCLC, EGFR	≥1	Osimeritinib	LCT	PFS
BRIGHTSTAR	NCT03707938	NSCLC, ALK	≥1	Brigatinib	LCT	Toxicity
HALT	NCT03256981	NSCLC with driver	1-3	TKI	RT	PFS

- *J Natl Compr Canc Netw 2022;20(5):531*

Patient Selection

An Individual Patient Data Metaanalysis of Outcomes and Prognostic Factors After Treatn of Oligometastatic Non–Small-Cell Lung Ca

Allison B. Ashworth,[1] Suresh Senan,[2] David A. Palma,[1] Marc Riquet,[3] Yong Chan Ahn,[4] Umberto Ricardi,[5] Maria T. Congedo,[6] Daniel R. Gon[7] Gavin M. Wright,[8] Giulio Melloni,[9] Michael T. Milano,[10] Claudio V. So[11] Tommaso M. De Pas,[12] Dennis L. Carter,[13] Andrew J. Warner,[1] George B. Rodrigues[1]

- Systematic review and Individual patient data meta analysis

- Low-risk disease: metachronous oligometastases, N0

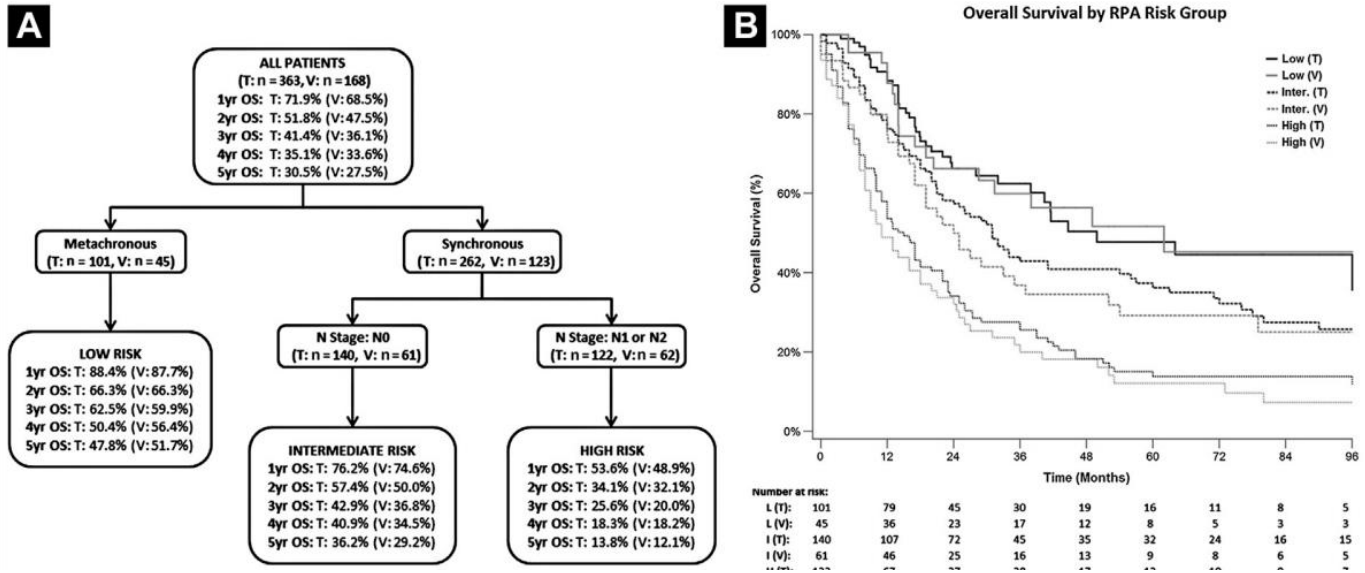
  ➔ 5 yr OS 47.8%

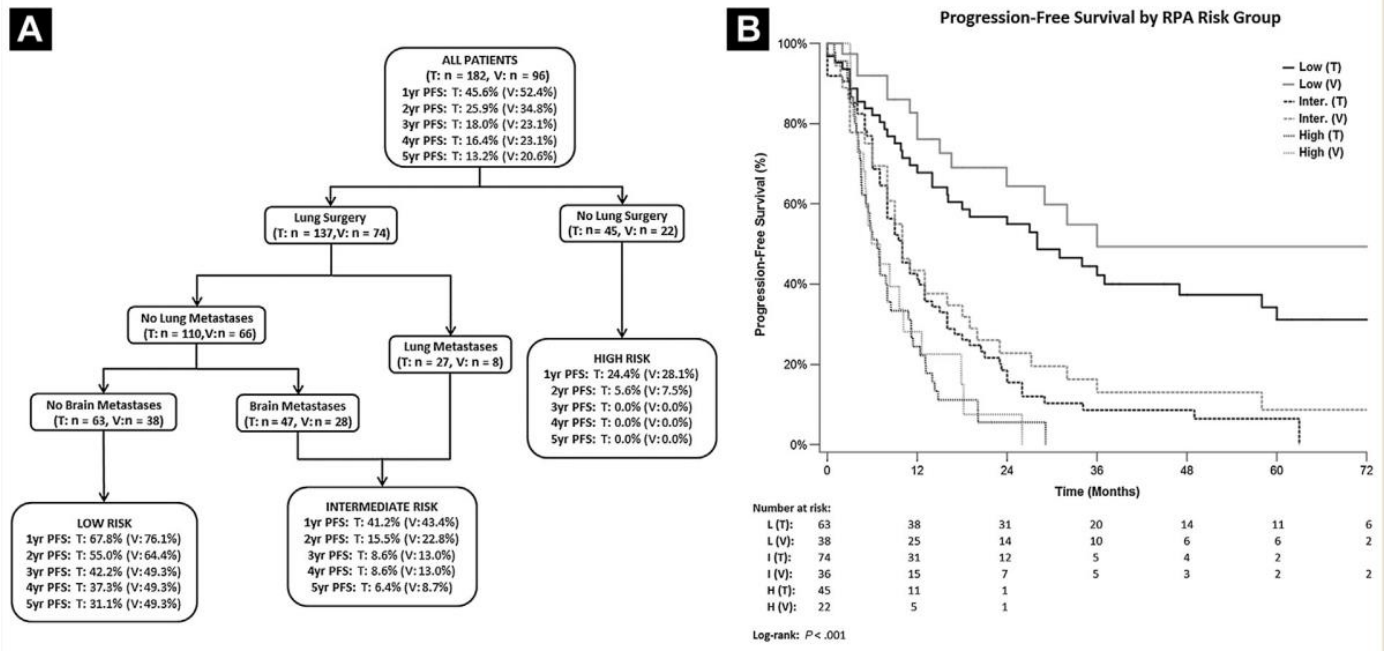
- Intermediate risk disease: synchronous oligometastases, N0

  ➔ 5 yr OS 36.2%

- High-risk disease: synchronous oligometastases, N1 or N2

  ➔ 5 yr OS 13.8%





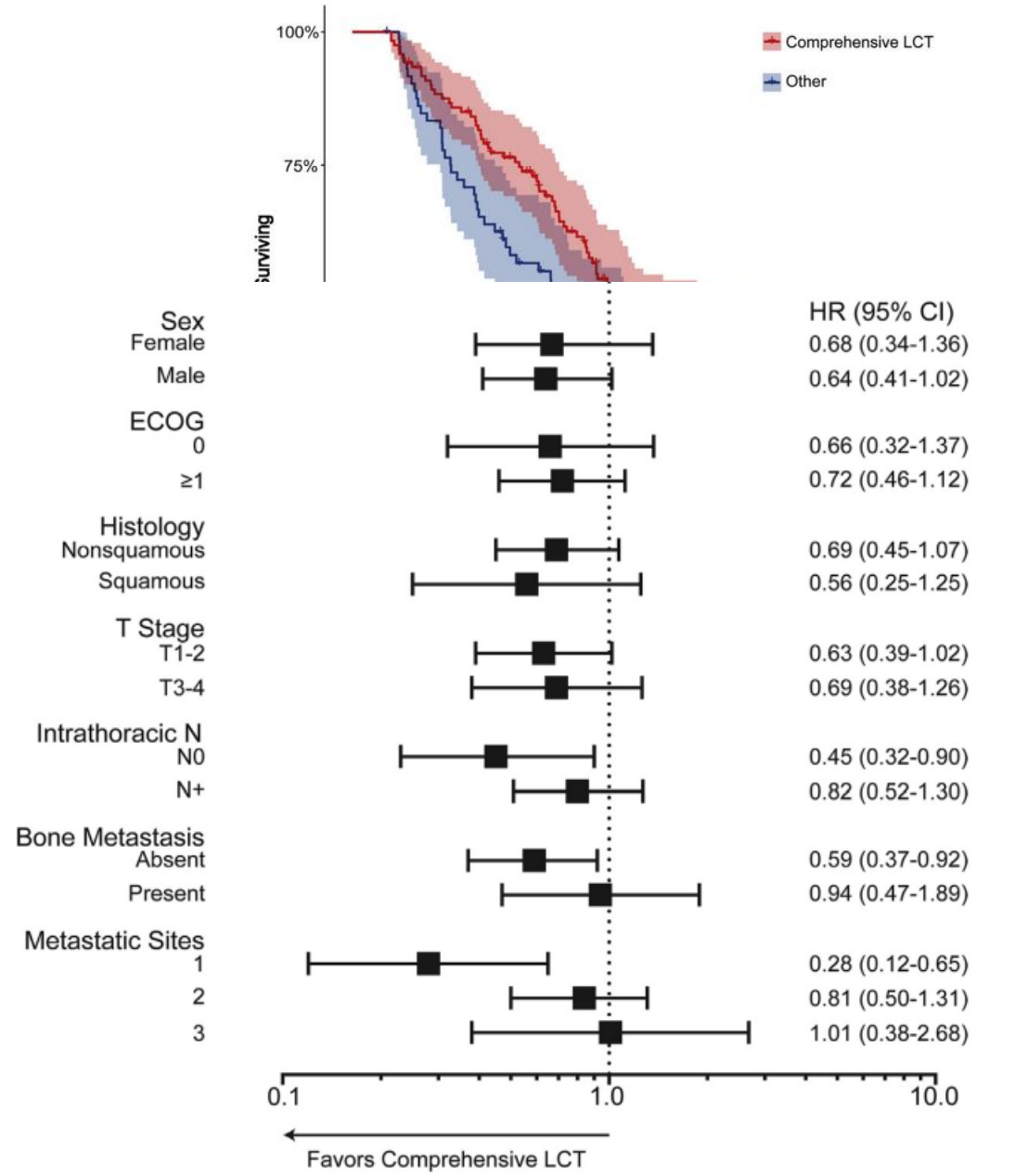
- *Clin Lung Cancer 2014;15:346*

Improved Overall Survival With Comprehensive Local Consolidative Therapy in Synchronous Oligometastatic Non–Small-Cell Lung Cancer

Kyle G. Mitchell,[1] Ahsan Farooqi,[2] Ethan B. Ludmir,[2] Erin M. Corsini,[1] Jiexin Zhang,[3] Boris Sepesi,[1] Ara A. Vaporciyan,[1] Stephen G. Swisher,[1] John V. Heymach,[4] Jianjun Zhang,[4] Daniel R. Gomez,[2] Mara B. Antonoff[1]

- Single center retrospective study
- 194 NSCLC, ≤3 synchronous oligometastatic lesions, 2000-2017

- Improved OS in LCT group: HR 0.67 (95% CI 0.47-0.97)
- Poor OS with thoracic nodal disease, bone metastases, or > 1 metastatic site
- Poor OS in LCT group: Squamous, intrathoracic disease burden, bone metastases



- ***Clin Lung Cancer 2019;21:37***

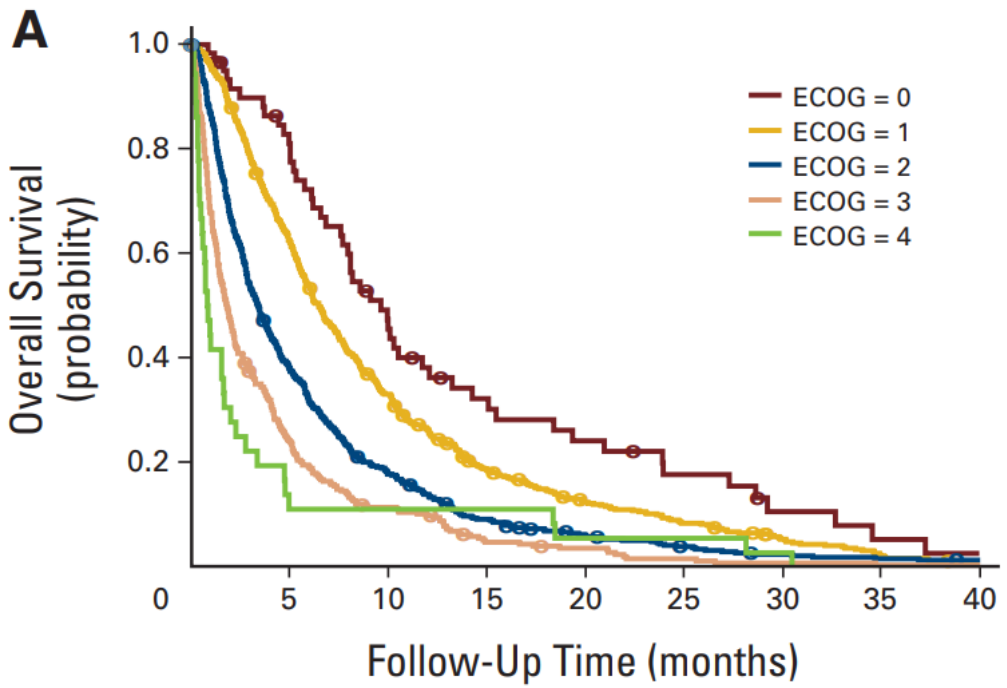
Simple Prognostic Model for Patients With Advanced Cancer Based on Performance Status

By Raymond W. Jang, MD, Valerie B. Caraiscos, MD, PhD, Nadia Swami, Subrata Banerjee, MD, Ernie Mak, MD, Ebru Kaya, MBBS, Gary Rodin, MD, John Bryson, MD, Julia Z. Ridley, MD, MEd, Lisa W. Le, and Camilla Zimmermann, MD, PhD

University of Toronto; and Princess Margaret Cancer Centre, University Health Network, Toronto, Ontario, Canada

- Retrospective study
- April 2007~February 2010
- 1,655 patients with advanced cancer

- ECOG 0: median OS 293 days (10 Mo)
- ECOG 1: median OS 197 days (6.5 Mo)
- ECOG 2: median OS of 104 days (3.5 Mo)
- ECOG 3: median OS of 55 days (2 Mo)
- ECOG 4: median OS of 25.5 days (1 Mo)



- *J Oncol Pract 2014;10(5):e335*

Patients Selection

	Patient Selection	Toxicity Risk	Timing
Best Candidates	Good performance status Low burden of disease (1 oligometastasis) Multiple systemic therapy options	Small lesions Treatment unlikely to cause toxicity (small resection or tumor far from critical structures)	Metachronous oligometastases Responding to systemic therapy
Less Favorable	Borderline performance status (ECOG 2) Moderate burden of disease (2-5 oligometastases)	Larger lesions Moderate risk of toxicity or impact on organ function	Synchronous oligometastases Overlapping toxicities (eg, immunotherapy and thoracic radiotherapy)
Unfavorable	Poor performance status (≥ECOG3) High burden of disease (> 5 metastases)	Very large lesions High risk of toxicity Comorbidities precluding radiotherapy or surgery	No response to systemic therapy Rapid disease progression

- ***J Clin Oncol 2022;40:635***

Modality of Local Therapy

Treatment Modality Selection

1. Tumor Location, Organ
2. Patient Fitness: Age, Perfomance, Comorbidity (Operability)
3. Patient Preference
4. Availability of Treatment Options

Prognostic factors of oligometastatic non-small-cell lung cancer following radical therapy: a multicentre analysis

Isabelle Opitz [a,*,†], Miriam Patella[a,†], Loic Payrard[b], Jean Yannis Perentes[b], Rolf Inderbitzi[c], Hans Gelpke[d], Sandra Schulte[d], Maja Diezi[a], Michel Gonzalez[b], Thorsten Krueger[b,‡] and Walter Weder[a,‡]

[a] Department of Thoracic Surgery, University Hospital of Zurich, Zurich, Switzerland
[b] Department of Thoracic Surgery, University Hospital of Vaudois, Lausanne, Switzerland
[c] Department of Thoracic Surgery, San Giovanni Hospital, Bellinzona, Switzerland
[d] Department of Thoracic and Visceral Surgery, Cantonal Hospital, Winterthur, Switzerland

- Multicenter, Retrospective study
- August 2001~February 2018
- ≤5 synchronous metastasis, ≤2 organs
- 124 NSCLC patients with radial resection

- 1, 2, 5-year OS: 80%, 58%, 36%
- Young age (≤60), pN0: good prognosis
- Bone metastasis: poor progrnosis

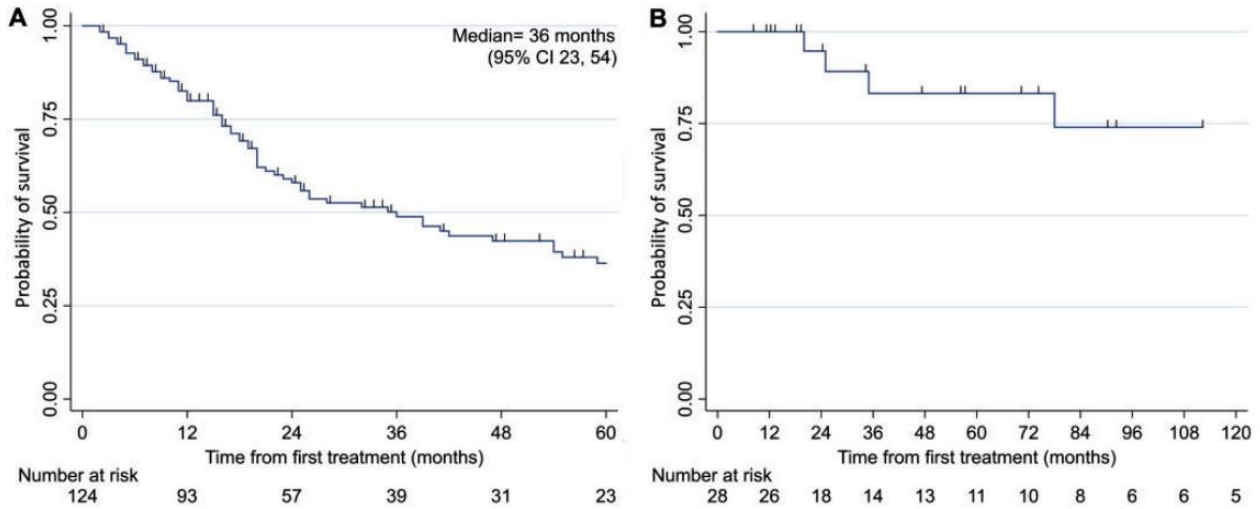


Figure 1: Survival curves for the entire population (**A**) and for patients ≤60 years and N0 (**B**). Median overall survival starting from primary tumour resection was 34 months (95% CI 22–51). CI: confidence interval.

Table 2: Results of Cox regression analysis for overall survival

Variables	HR	95% CI	*P*-value
Age ≤ 60 years versus >60 years	0.41	0.24–0.69	0.001
pN0 versus pN1–2	0.38	0.21–0.69	0.002
Metastasis location			
Bone versus other	2.53	1.05–6.09	0.04
Lung versus other	0.18	0.02–1.45	0.1

CI: confidence interval; HR: hazard ratio.

Table 4: Results of Cox regression analysis for progression-free survival

Variables	HR	95% CI	*P*-value
Metastasis first	0.59	0.34–1.04	0.09
pN0 versus pN1–2	0.38	0.41–0.10	<0.001
Metastasis location			
Bone versus other	1.88	1.06–3.34	0.04
Brain versus other	2.02	0.87–4.74	0.1

CI: confidence interval; HR: hazard ratio.

- ***Eur J Cardiothorac Surg 2020;57:1166***

Safety and Survival Rates Associated With Ablative Stereotactic Radiotherapy for Patients With Oligometastatic Cancer

A Systematic Review and Meta-analysis

Eric J. Lehrer, MD, MS; Raj Singh, MD; Ming Wang, MS, PhD; Vernon M. Chinchilli, PhD; Daniel M. Trifiletti, MD; Piet Ost, MD, PhD; Shankar Siva, PhD, MBBS; Mao-bin Meng, MD, PhD; Leila Tchelebi, MD; Nicholas G. Zaorsky, MD, MS

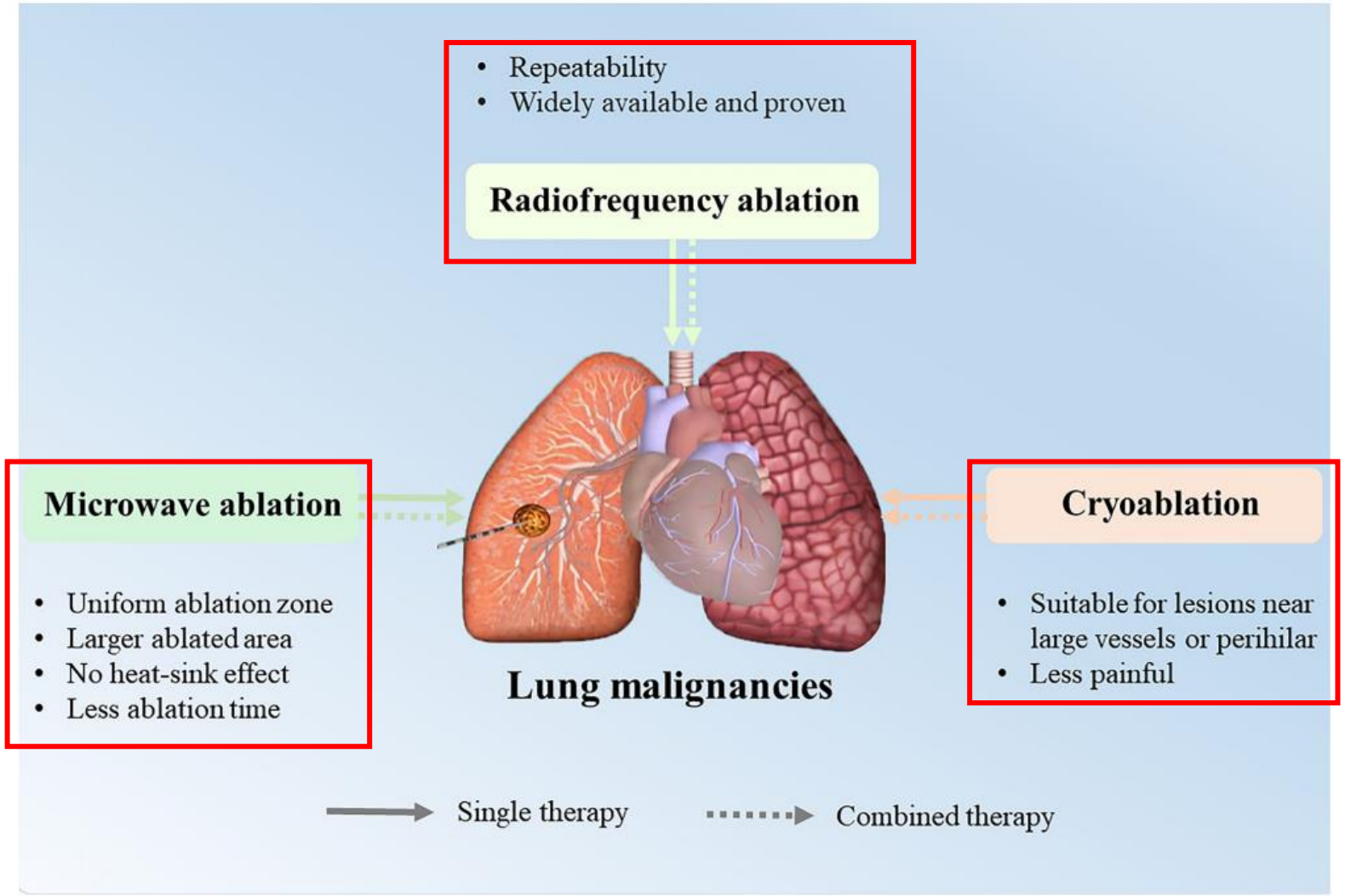
- Systematic review and Meta analysis
- Single or multiple arm prospective trials
- ≤5 sites of extracranial oligometastasis
- SABR: ≤ 8 fractions, ≥ 5 Gy/fraction
- 943 patients and 1290 oligometastases were included
- Prostate (22.9%), Colorectal (16.6%), Breast (13.1%), Lung (12.8%)

- Acute Toxicity: Gr3-5 1.2% (95% CI, 0%-3.8%)
- Late Toxicity: Gr3-5 1.7% (95% CI, 0.2%-4.6%)
- 1-year local control rate: 94.7% (95% CI, 88.6%-98.6%
- 1-year PFS: 51.4% (95% CI, 42.7%-60.1%)
- 1-year OS: 85.4% (95% CI, 77.1%-92.0%)

1. Underlying comorbidities: ILD, CTD
2. Large sized tumor >5cm
3. Difficult to distinguish the fibrotic change and recurrence

- *JAMA Oncol 2021;7(1):92*

Modality of Local Ablative Therapy



- *Front Oncol 2022;10:1020296*

Percutaneous ablation

Table 1
Results of cohort studies evaluating outcomes for patients with early-stage NSCLC treated with thermal ablation techniques.[a]Overall survival includes 19 patients with controlled non-progressive extra-thoracic metastatic disease (Stage IV) and 2 patients with Stage IIIa disease, all node negative. [b]Includes patients with Stage IIb-IV disease without nodal or metastatic disease. [c]Included 4 small cell lung cancer (SCLC). [d]In those with local recurrence [e]In those without local recurrence.

Author, date	Ablation modality	Stage I/IIA NSCLC patient cohort size, number of lesions	Tumor size (cm) (mean, unless otherwise stated)	2-year survival %	5-year survival %	Local recurrence rate (%)
Simon et al., 2007 [32]	RFA	75, 80	3.0	57.0	27.0	NR
Hiraki et al., 2007 [33]	RFA	20, NR	2.4	84.0	NR	7/20 (35.0)
Lanuti et al., 2009 [34]	RFA	31, 38	2.0	78.0	NR	12/38 (31.5)
Ambrogi et al., 2011 [35]	RFA	57, 59	2.6	NR	25.0	13/59 (22.0)
Hiraki et al., 2011 [36]	RFA	50, 52	2.1	86	NR	16/52 (30.7)
Yamauchi et al., 2012 [37]	Cryoablation	22, 34	1.4	88	NR	1/34 (2.9)
Lanuti et al., 2012 [38]	RFA	45, 55	2.3	NR	31.0	18/55 (32.7)
Yang et al., 2014 [39]	MWA	47, 47	NR	63.0	16.0	13/47 (27.7)
Han et al., 2015 [40]	MWA	28, 28	NR	76.5	NR	9/28 (32.1)
Palussiere et al. 2015 [41]	RFA/MWA	66, NR	2.1 (median)	77.5[a]	58.1[a]	14/87 (16.1)
Moore et al. 2015 [42]	Cryoablation	45, 47	1.9	NR	67.8	7/47 (15.8)
Zheng et al., 2016 [43]	MWA	52, 52[b]	NR	82.4[b]	NR	NR
Zhong et al., 2017 [44]	MWA	35, 35	3.1 (median)	94.1	NR	2/35 (5.7)
Narsule et al., 2017 [45]	RFA/MWA	21, 21 (RFA) 4(MWA)	1.9	81.0	NR	10/21 (47.6)
Yang et al., 2017 [46]	MWA	104, 104[c]	2.3	79.6[d], 69.5[e]	27.0[d], 26.1[e]	24/104 (23.1)
Huang et al., 2018 [47]	RFA	50, 73	2.2	86.5	36.3	13/50 (26.0)
Han et al., 2019 [48]	MWA	63, 65	2.7	92.6	32.6	14/63 (22.2)
Zhao et al., 2020 [49]	MWA	34, 34	2.6 (median)	66.7	46.7	10/34 (29.4)
Nomori et al., 2020 [50]	Cryoablation	101, 101	1.4	NR	NR	10/101 (9.9)
Nance et al., 2021 [51]	MWA	21, 21	1.7	61.8	45.7	2/20 (10.0)

- ***Lung Cancer 2023;176:14***

Local Ablative Therapy

TABLE 3: Role of Percutaneous IGTA in the Management of NSCLC Based on Current Guidelines

Source	Year(s)[a]	Disease Stage	Qualification Regarding Ablative Therapy
SIR [1]	2021	Stage 1A	Safe and effective treatment with minimal complications and survival outcomes comparable to SBRT and sublobar resection
		Recurrent	Safe and effective treatment option
NCCN [5]	2020	Stage IA T1–T3N0	Option for selected patients with peripheral tumors categorized as T1abcN0 disease Option for selected patients
		Multiple Locoregional recurrence	Option for asymptomatic solitary metachronous tumor Option for selected patients, including those with disease progression on EGFR or ALK therapy
CIRSE [2]	2020	Stage I	Option for patients with contraindications to surgery and curative-intent option for patients with category T1a or T1b disease
		Other stages	Option for patients with contraindications to surgery or SBRT
ESMO [3]	2017	Stage I	Option for patients with contraindications to surgery or SBRT
ACCP and STS [4]	2012, 2013	Stage I	Option for patients with peripheral tumor measuring < 3 cm

Note—IGTA = image-guided thermal ablation, NSCLC = non–small cell lung cancer, SIR = Society of Interventional Radiology, SBRT = stereotactic body radiotherapy, NCCN = National Comprehensive Cancer Network, EGFR = epidermal growth factor receptor, ALK = anaplastic lymphoma kinase, CIRSE = Cardiovascular and Interventional Radiological Society of Europe, ESMO = European Society for Medical Oncology, ACCP = American College of Chest Physicians, STS = Society of Thoracic Surgeons.

[a]Multiple years are listed if referencing multiple guidelines.

- *AJR 2022;219:471*

Navigation Bronchoscopy-Guided Radiofrequency Ablation for Nonsurgical Peripheral Pulmonary Tumors

Fangfang Xie[a, b] Xiaoxuan Zheng[a] Bo Xiao[c] Baohui Han[b] Felix J.F. Herth[d]
Jiayuan Sun[a, b]

Departments of [a]
and [c]Medsphere
Medicine, Transl
University of Hei

Transbronchial microwave ablation of lung nodules with electromagnetic navigation bronchoscopy guidance—a novel technique and initial experience with 30 cases

Joyce W. Y. (
Tony S. K. M

Electromagnetic bronchoscopy guided microwave ablation for early stage lung cancer presenting as ground glass nodule

Feichao Bao#, Fengha
Xiuxiu Hao, Zhitao G

Endobronchial ultrasound-guided bipolar radiofrequency ablation for lung cancer: A first-in-human clinical trial

Tsukasa Ishiwata, MD, PhD,[a] Yamato Motooka, MD, PhD,[a] Hideki Ujiie, MD, PhD,[a] Terunaga Inage, MD, PhD,[a] Alexander Gregor, MD,[a] Masato Aragaki, MD, PhD,[a] Zhenchian Chen, MD,[a] Tomonari Kinoshita, MD, PhD,[a] Laura Donahoe, MD, MSc,[a] Jonathan Yeung, MD, PhD,[a] Marcelo Cypel, MD, MSc,[a] Marc de Perrot, MD, MSc,[a] Andrew Pierre, MD, MSc,[a] Gail Darling, MD,[a] Thomas Waddell, MD, PhD,[a] Shaf Keshavjee, MD, MSc,[a] Prodipto Pal, MD, PhD,[b] and Kazuhiro Yasufuku, MD, PhD[a]

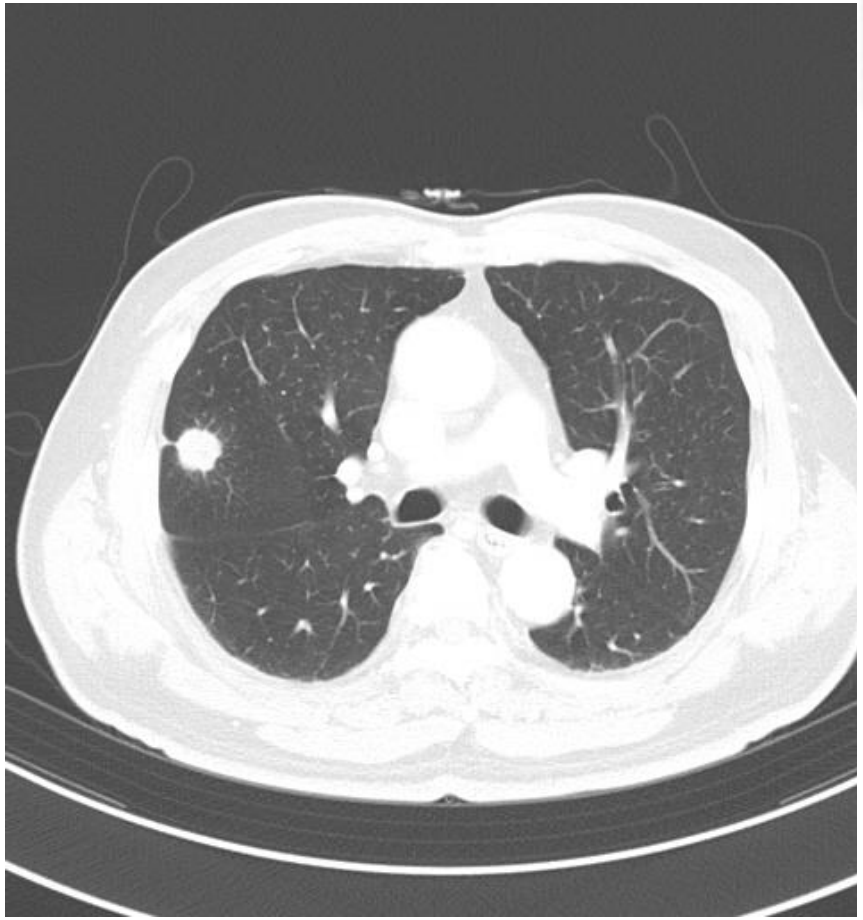
- ***Respiration 2017;94:293***
- ***Transl Lung Cancer Res 2021;10:1608***
- ***Transl Lung Cancer Res 2021;10:3759***
- ***J Thorac Cardiovasc Surg 2022;164:1188***

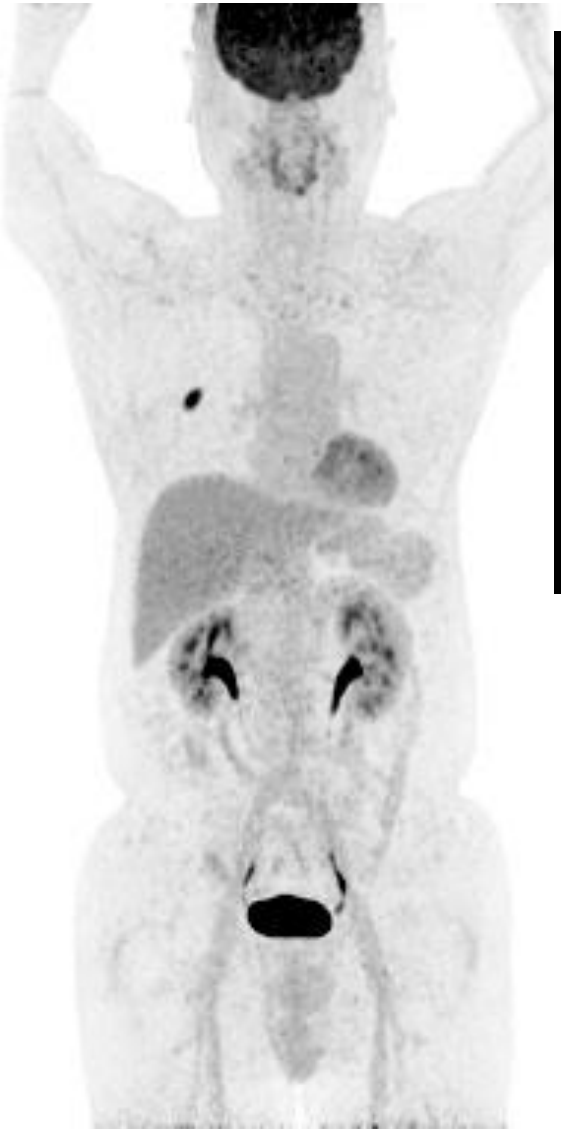
Modality of Local Therapy

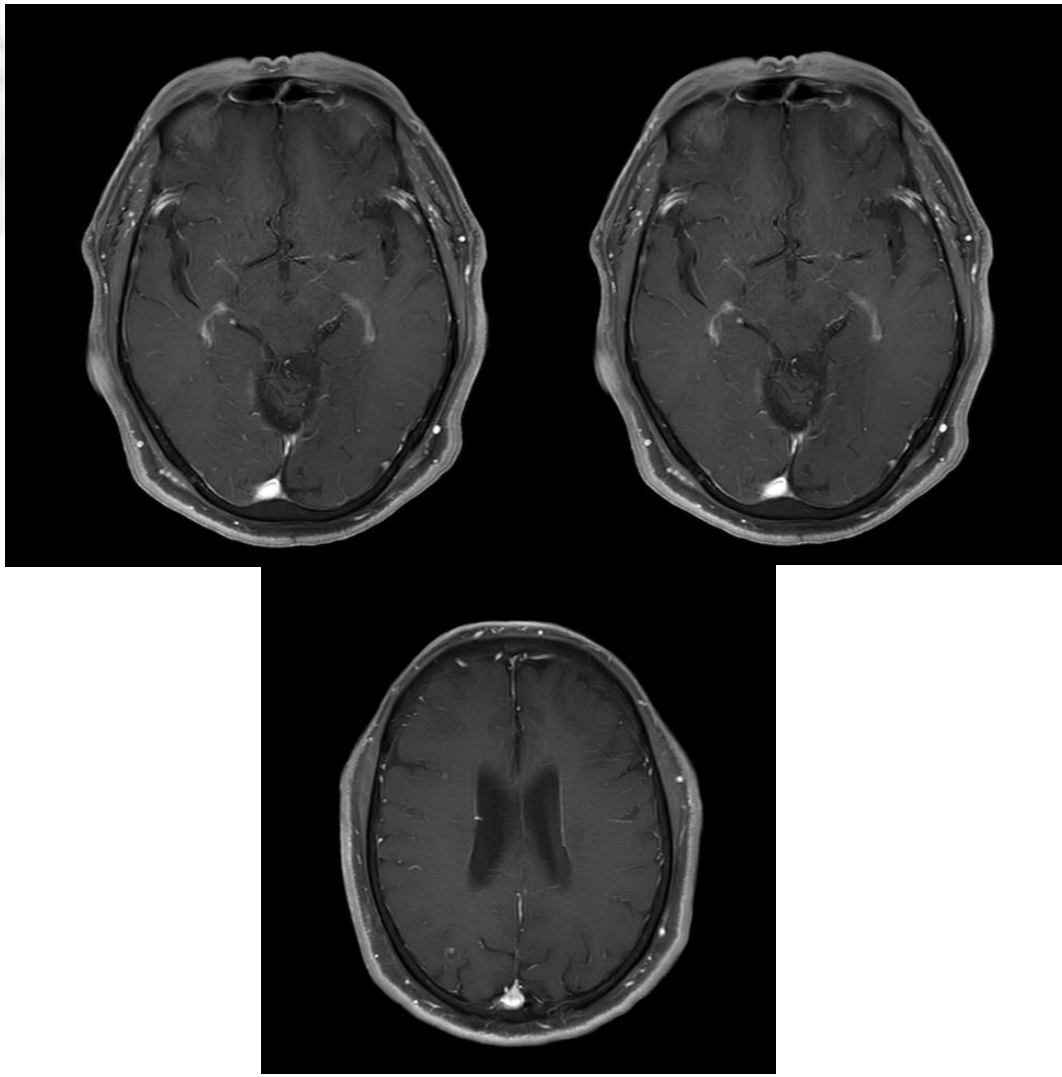
Characteristic	Surgery	IGTA	SBRT
No of visits	1	1	Usually 4-6
Potential complications	Pneumothorax BPF, Bleeding Pneumonia, Pain	Pneumothorax BPF, Bleeding	Pneumonitis Pain, Esophagitis, Cardiac toxicity
Ability to concurrently obtain tissue from tumor	Yes	Yes	No
Interruption of systemic therapy required	Yes	No (with respect to targeted therapy and IO)	Possibly (if pneumonitis develops)
Measurable long-term reduction of lung function	Yes	No	Yes (moderate)
Repeatability of treatment	Limited	Yes	Limited
Imaging follow-up required	Yes	Yes	Yes

- *AJR 2022;219:471*

Case 1 70/M NSCLC ADC RUL cT1cN0M1c







이 환자의 진단은?

1. **Synchronous oligometastasis**
2. Metachronous oligometastasis
3. Oligoprogression
4. Oligorecurrence

다학제 논의

- 원칙적으로 brain mets가 있어 stage IV lung cancer로 수술적 치료가 교과서적인 치료는 아니나, (재발의 위험성이 높음)

- 환자 PS가 양호하며, tumor burden이 적고 oligometastasis인 상태이므로 LCT가 생존의 이득이 있을수 있음을 설명함.

- 환자가 적극적인 LCT에 동의하면 brain mets에 대해 GKRS 시행 및 Lung에 대해서도 수술 가능함을 설명함

➔ 환자 적극적 치료 원하여 GKRS+OP 시행함

수술기록

- Pleural nodules 은 chest wall 곳곳에서 발견할 수 있었으며, 개개의 크기는 several mm 정도로 크지 않았음

- Pleural biopsy 후 frozen에서 malignant (+) 로 확인되어, RML lobectomy 대신 wide wedge 시행 후 종료함

임상경과

NSCLC, ADC, M/D, RML with pleural seeding, brain mets

- EGFR 19del+, ALK-, PD-L1 SP263 5%, PD-L1 22C3 20%

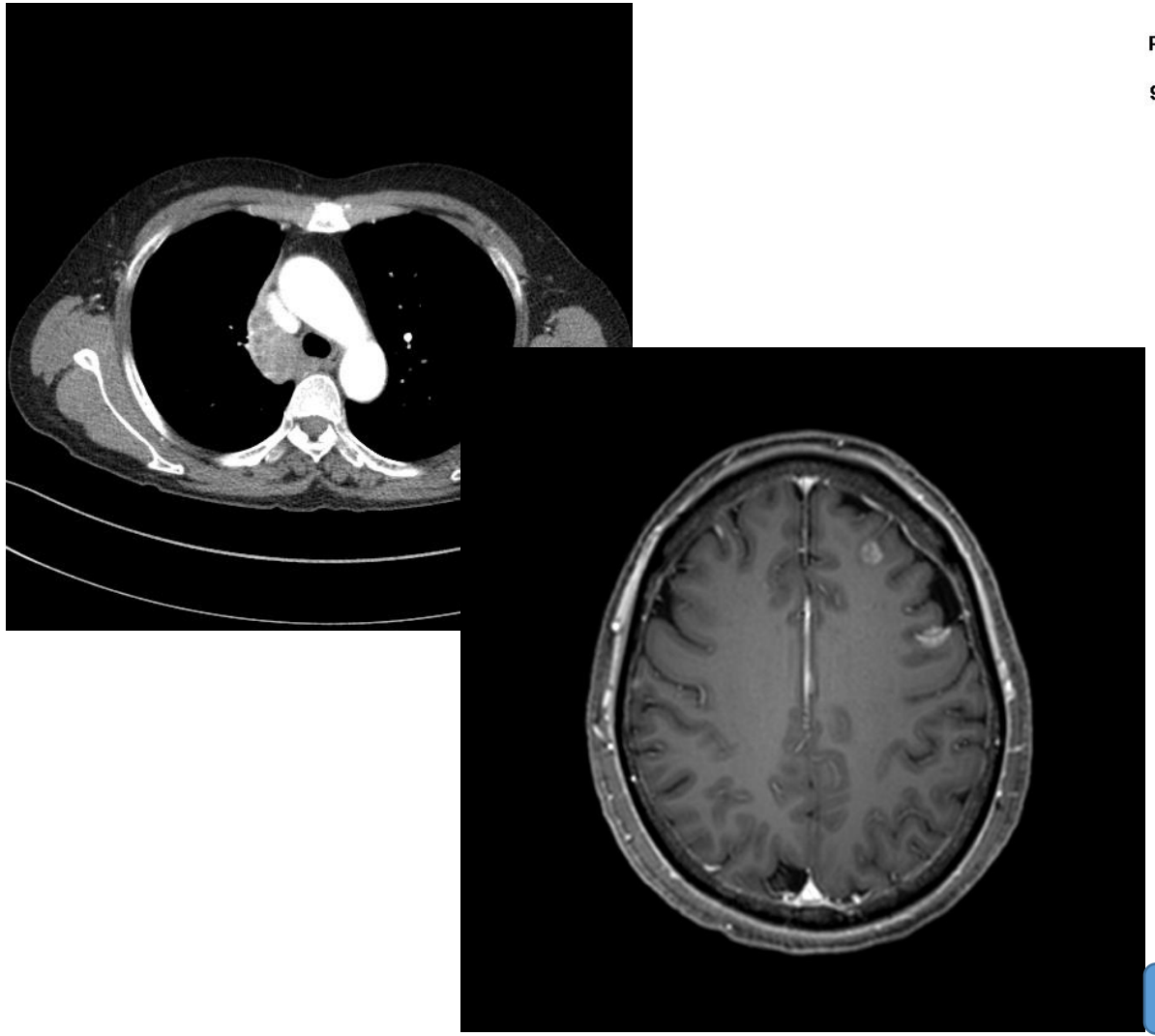
s/p wedge, RML, VATS (200219)

on Iressa (20.02.22-)

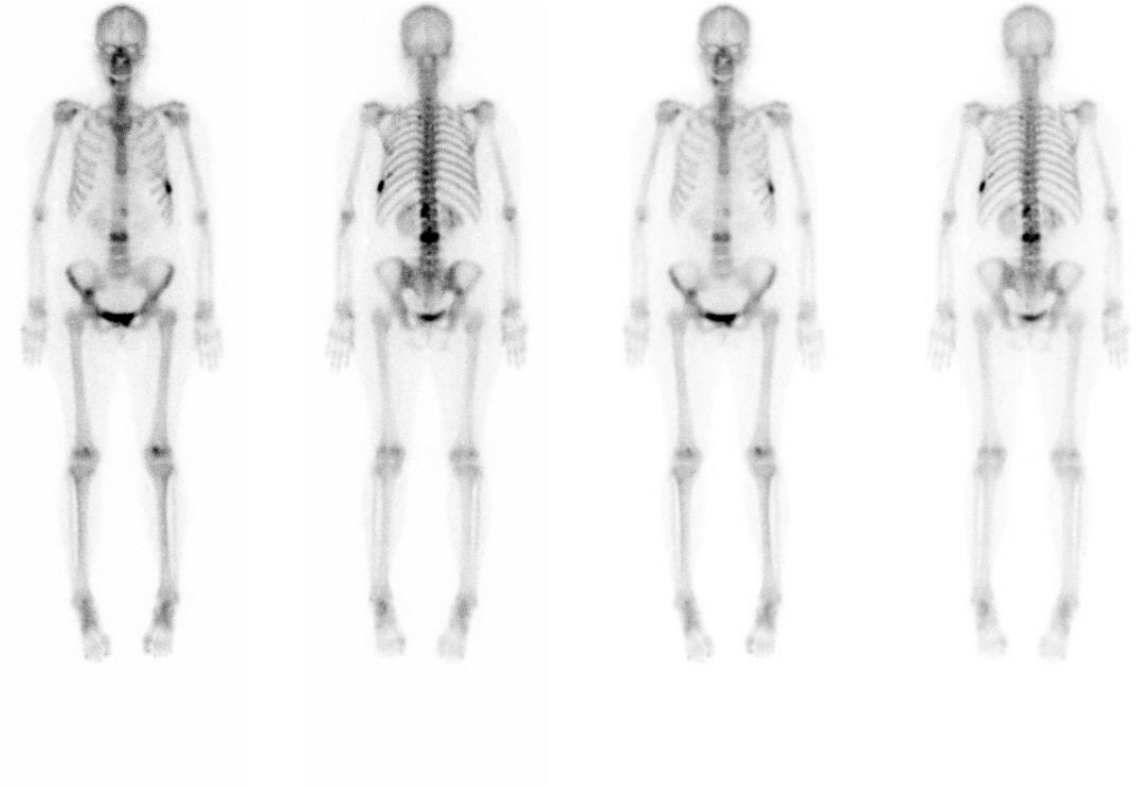
Multiple brain metastasis, Rt. parietal, Lt. parietotemporal, Rt. occipital lobes

s/p GKRS (20.03.09)

Case 2 60/F NSCLC ADC cT4N2M1c

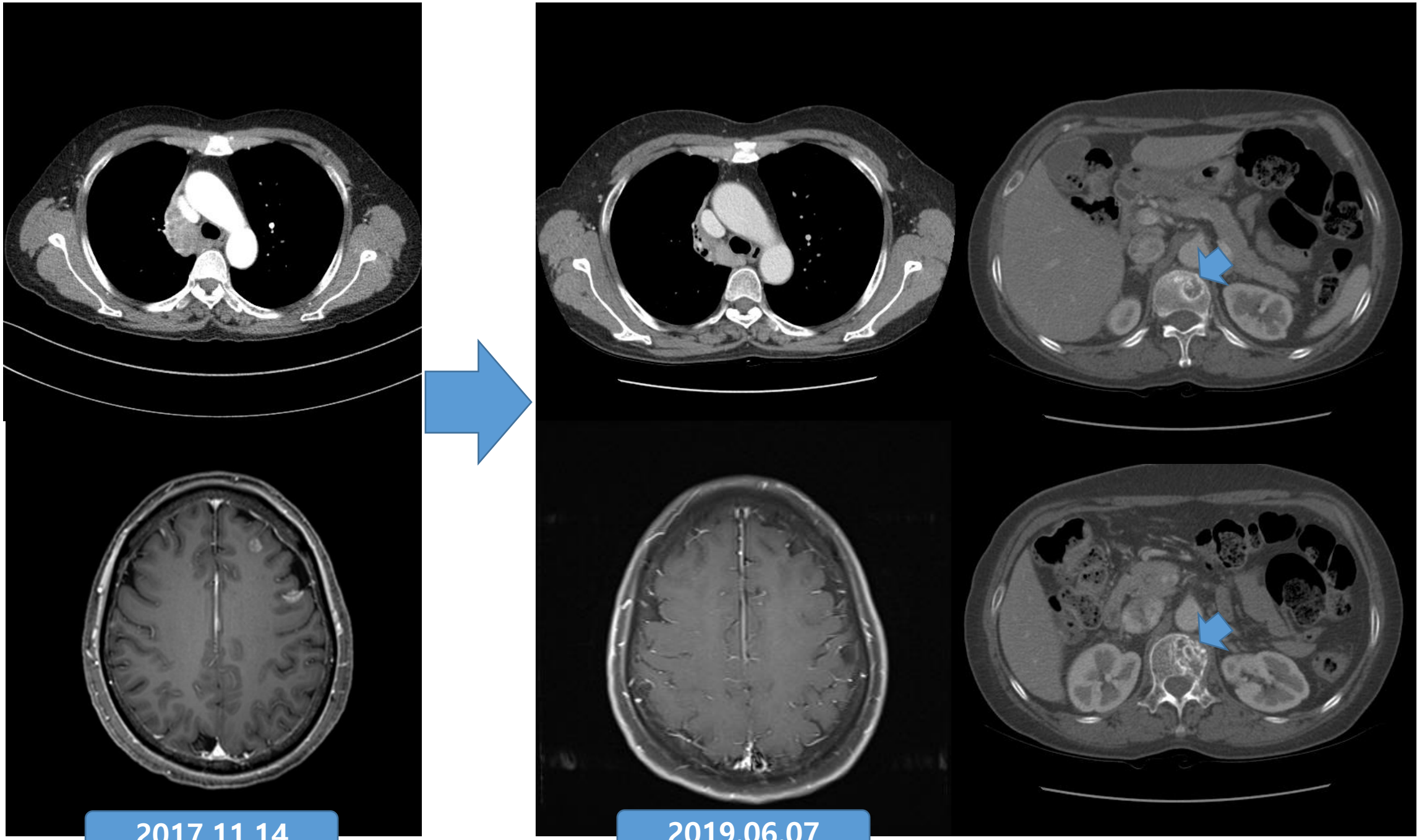


Patient Name: KIM SOONDEOK, F62 Patient ID: 53803708 Study Name: Bone Scan
Study Date: 11/1/2017
99mTc-DPD Whole Body Bone Scan Oncoflash Post I.V 3 hrs 31 min



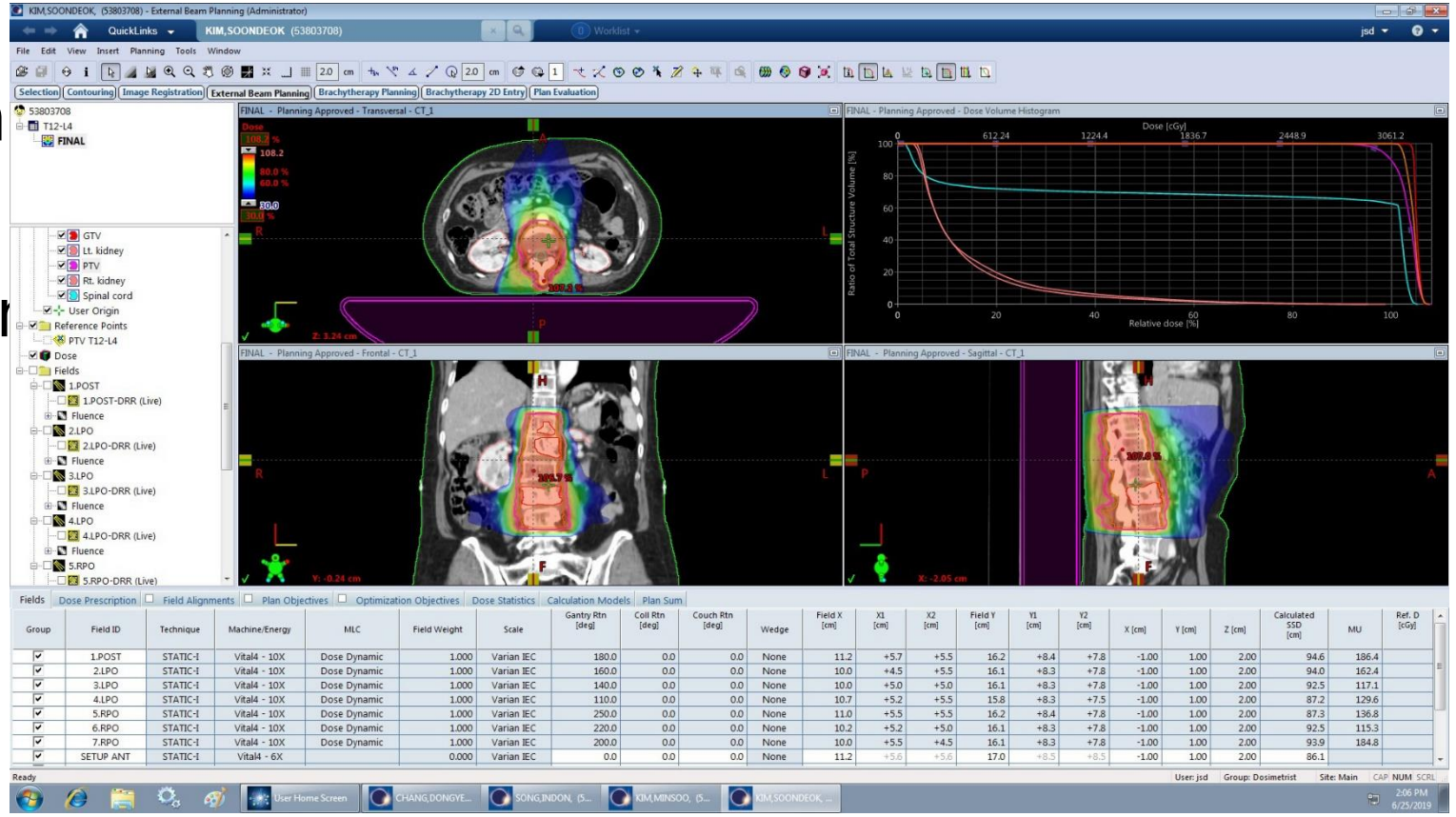
ANTERIOR 1482K Counts | POSTERIOR 1419K Counts | ANTERIOR 1482K Counts | POSTERIOR 1419K Counts

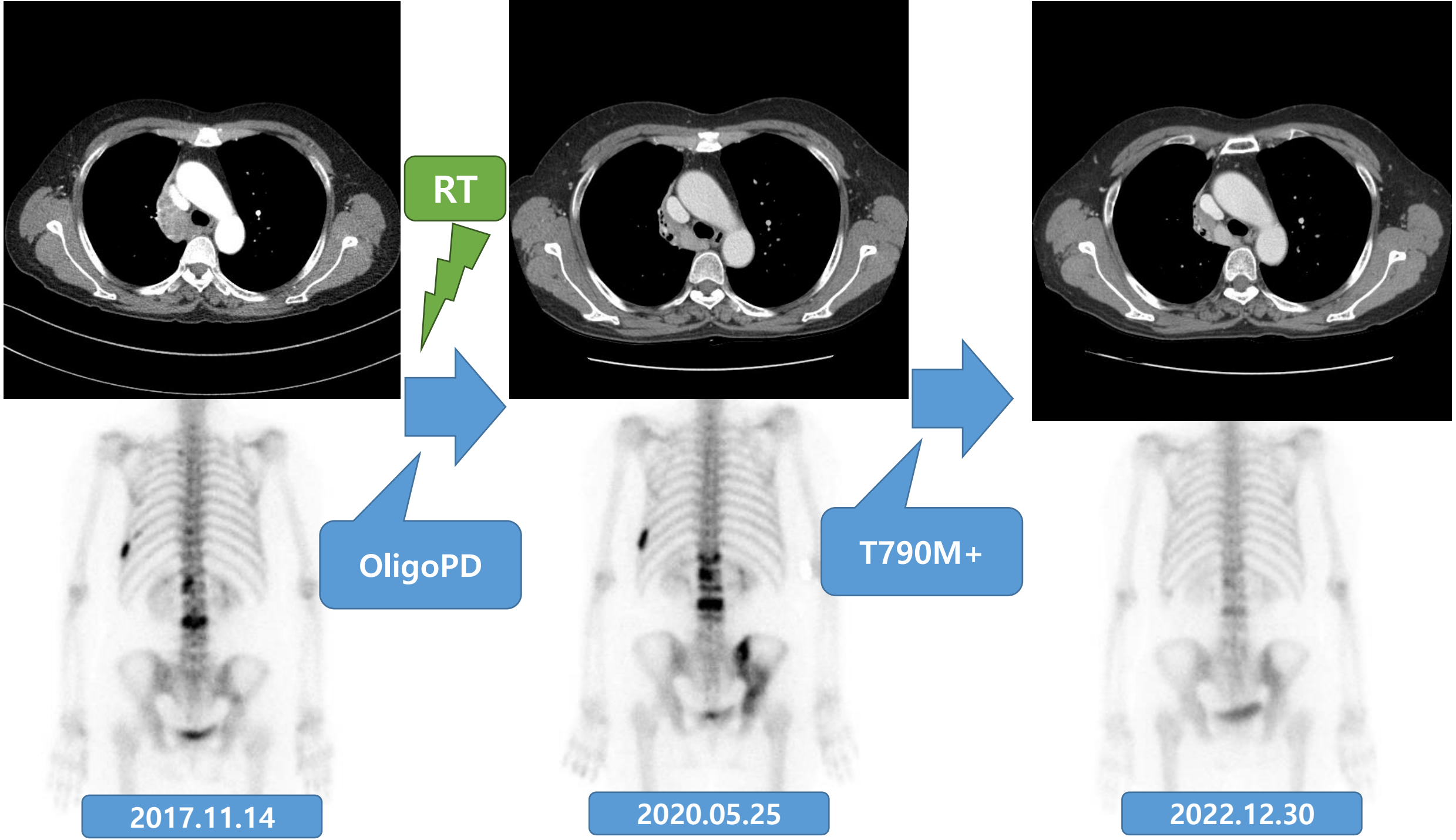
EGFR 19del+


2017.11.14
2019.06.07

이 환자의 진단은?　　치료는?

1. Synchronous oligom
2. Metachronous oligor
3. **Oligoprogression**
4. Oligopersistance




RT
OligoPD
T790M+
2017.11.14
2020.05.25
2022.12.30

Summary

1. **Classification of OMD: ≤5 metastasis site, ≤ 3 organ**
   - **Synchronous OMD (or de novo OMD)**
   - **Metachronous OMD (or Oligorecurrence): > 3 or 6 months**
   - **Oligoprogression**
   - **Oligopersistence**
2. **Clinical Evidences**
   - **4 major RCT showed significant improvement of PFS, OS**
   - **Many ongoing clinical trials**

Summary

3. **Patient Selection**
    - **Good Performance Status**
    - **Low Tumor Burden**
    - **Effective Systematic Therapy**
4. **Modality of Local Therapy**
    - **Surgery**
    - **Radiation Therapy (SBRT)**
    - **Local Ablative Therapy**

경청해 주셔서 감사합니다.

서울아산병원
Asan Medical Center