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제11회 폐암 심포지엄

Response Evaluation of Chemotherapy for Lung cancer

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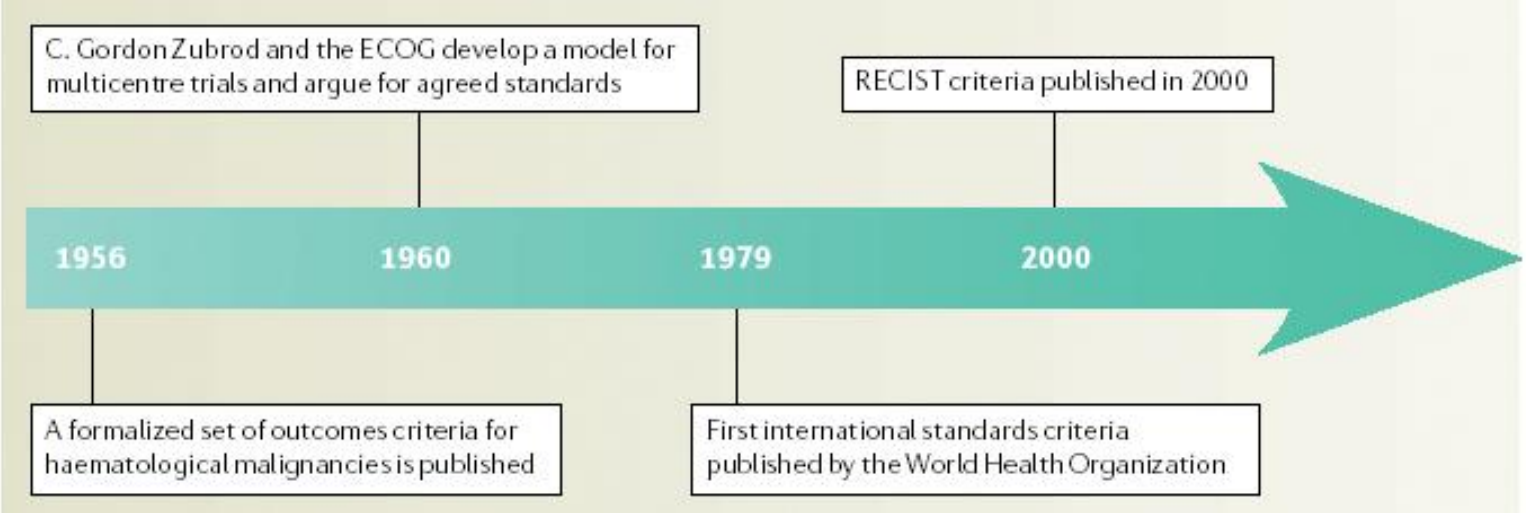
CONTENT

Background

❖ **Assessing response to therapy allows for :**

- Prospective end point evaluation in clinical trials
- Serve as a guide for decision making for clinician

❖ **Documenting response of cancer to therapy**



Nature Reviews Cancer ***6****, 409-414 (2006)*

Development of Response Evaluation Criteria for Solid Tumors (RECIST)

- 1994 international task force
  - European Organization for Research and Treatment of Cancer (EORTC)
  - National Cancer Institute (NCI) of the U.S.
  - National Cancer Institute of Canada Clinical Trials Group
- Review of 4000 patients for tumor response
- 1999: Criteria was publicly presented/accepted the American Society for Clinical Oncology meeting
- 2000: Published in Journal of the National Cancer Institute
- Intended for solid tumor response assessment in Phase II clinical trials but is actually being used for response assessment in all Phases

WHO
Response Criteria
1979

RECIST
Response Criteria
2000

Issue in WHO response criteria

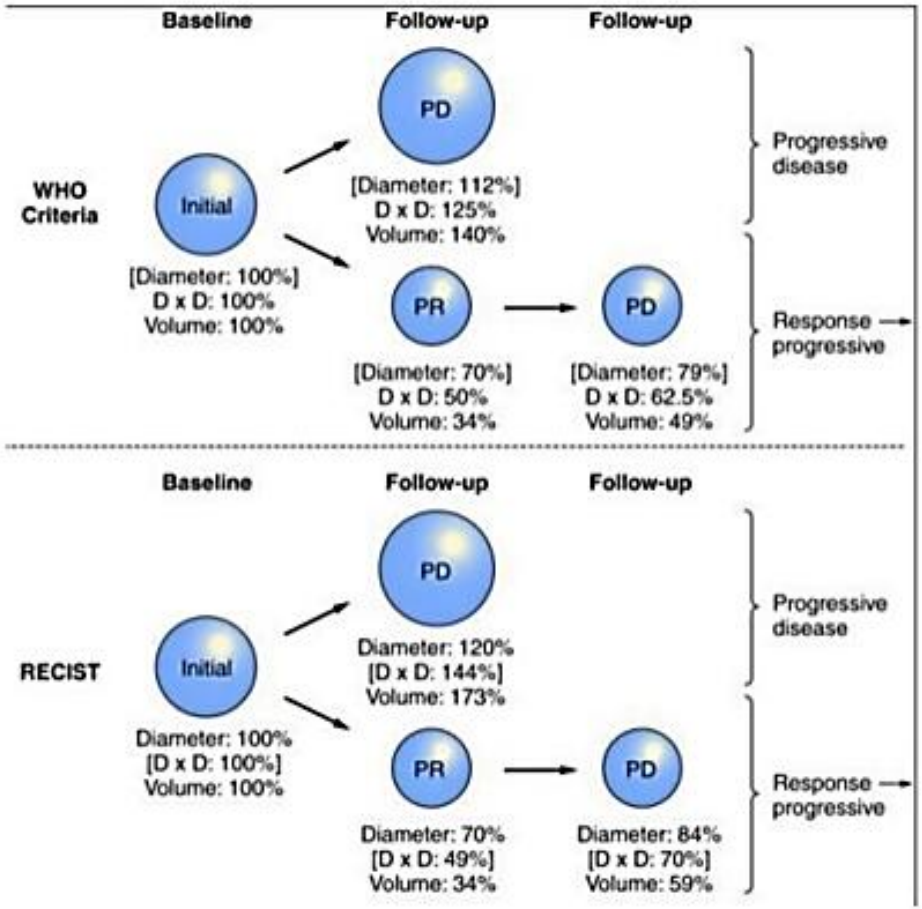
1) Complexity
- Needs bi-dimensional measurements
- No minimum lesion size & number
- Results may vary among research groups

2) New technologies

3) No longer regarded

http://www.irrecist.com/recist/recist-comparative

WHO vs RECIST



- 33% higher threshold to meet PD
- PR definitions are almost identical

Health and medicine, sep 30, 2012 Clinical response evaluation

RECIST 1.0
Response Criteria
2000

RECIST 1.1
Response Criteria
2009

1) Number of target lesions
2) Assessment of pathologic LN
3) Clarification of disease progression
4) Clarification of unequivocal progression of non-target lesions
5) Inclusion of ^{18}F-FDG PET in the detection of new lesions

http://www.irrecist.com/recist/recist-comparative

RECIST v1.1 IS PERFECT ?

Measurability of Tumors at Baseline

RECIST 1.0

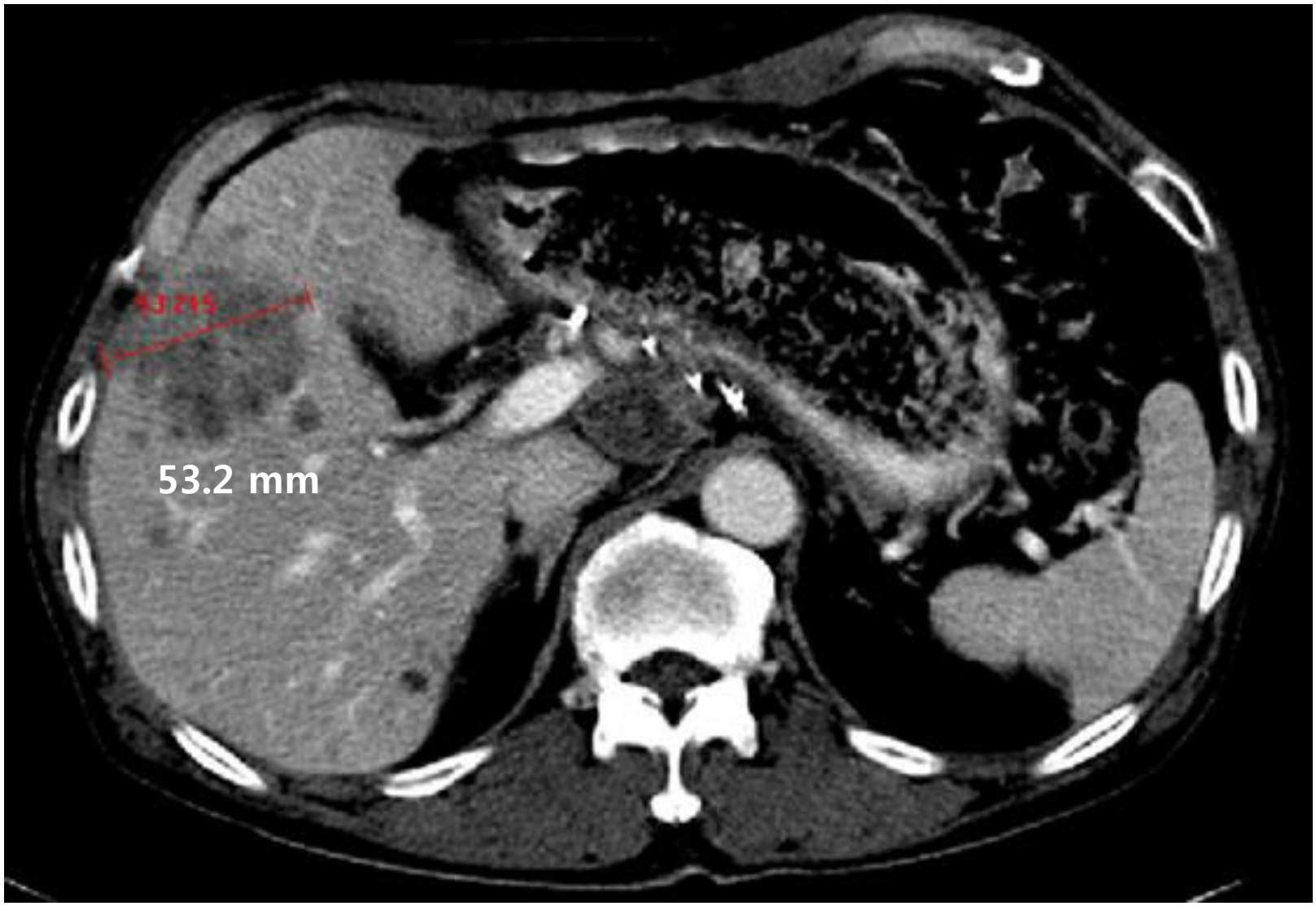
- At baseline, measurable tumor lesions that can be accurately measured in at least one dimension (longest diameter) as
  - ≥ 20 mm with conventional techniques or
  - ≥ 10 mm with spiral CT scan

RECIST 1.1

- Must be accurately measured in at least one dimension (longest diameter in the plane) with a minimum size of:
  - **10 mm by CT scan and MRI**
  - **10 mm caliper measurement by clinical exam (when superficial)**
  - **20 mm by chest X-ray**

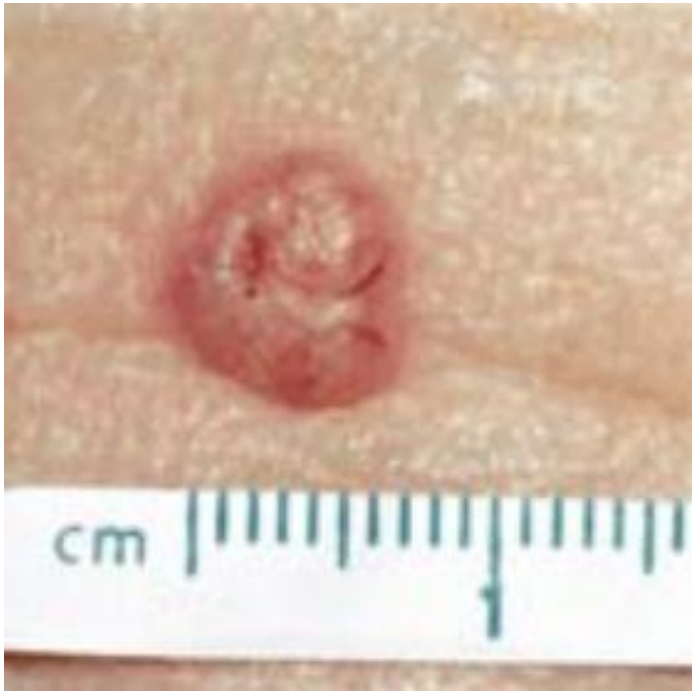
    (if clearly defined and surrounded by aerated lung)

Measure the Longest in Plane Diameter



Clinical Exam may be Used to Follow Superficial Lesions Over Time

- Recommended that skin lesion assessment include taking a lesion color picture with a ruler to document the size of the lesion



Non-measurable Lesions

RECIST 1.0

- All other lesions
- Include
  - Bone lesions
  - Leptomeningeal disease
  - Ascites
  - Pleural/pericardial effusion
  - Inflammatory breast disease
  - Lymphangitis cutis/pulmonis
  - Abdominal masses that are not confirmed and followed by imaging techniques
  - Cystic lesions

RECIST 1.1

- All other lesions
  - Pleural or pericardial effusion
  - Ascites
  - Inflammatory breast disease
  - Lymphangitis cutis/pulmonis
  - Leptomeningeal disease

- **Bone and cystic lesions removed**
- **Organomegaly added**

Bone Lesion Measurability

RECIST 1.0

- Non-measurable Lesions

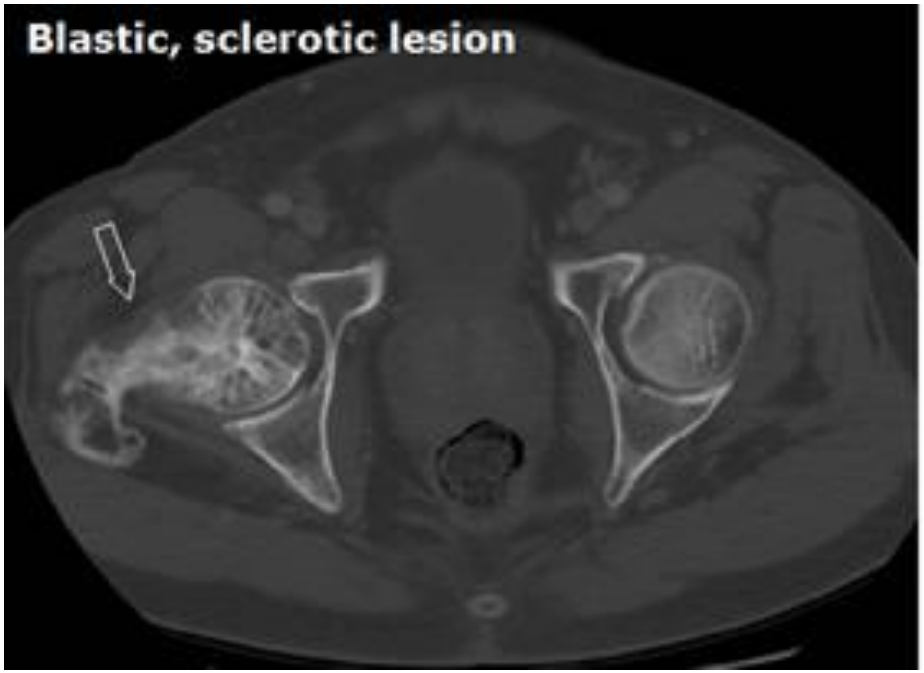
RECIST 1.1

- **Lytic bone lesions, with an identifiable soft tissue component,** evaluated by CT or MRI, **can be considered as measurable lesions**

- **Blastic bone lesions are non-measurable**

Bone metastasis

- Lytic bone lesions, with an identifiable soft tissue component, evaluated by CT or MRI, can be considered as measurable lesions
- Blastic bone lesions are non-measurable



Cystic Lesion Measurability

RECIST 1.0

- Non-measurable Lesions

RECIST 1.1

- No simple cysts
- **Radiographically indeterminate, complex "cystic" lesions** should be considered **non-measurable lesions**
- **“Cystic lesions" thought to be cystic metastases** can be considered as **measurable lesions**

Assessment of Lymph Nodes

RECIST 1.0

- No specific recommendations

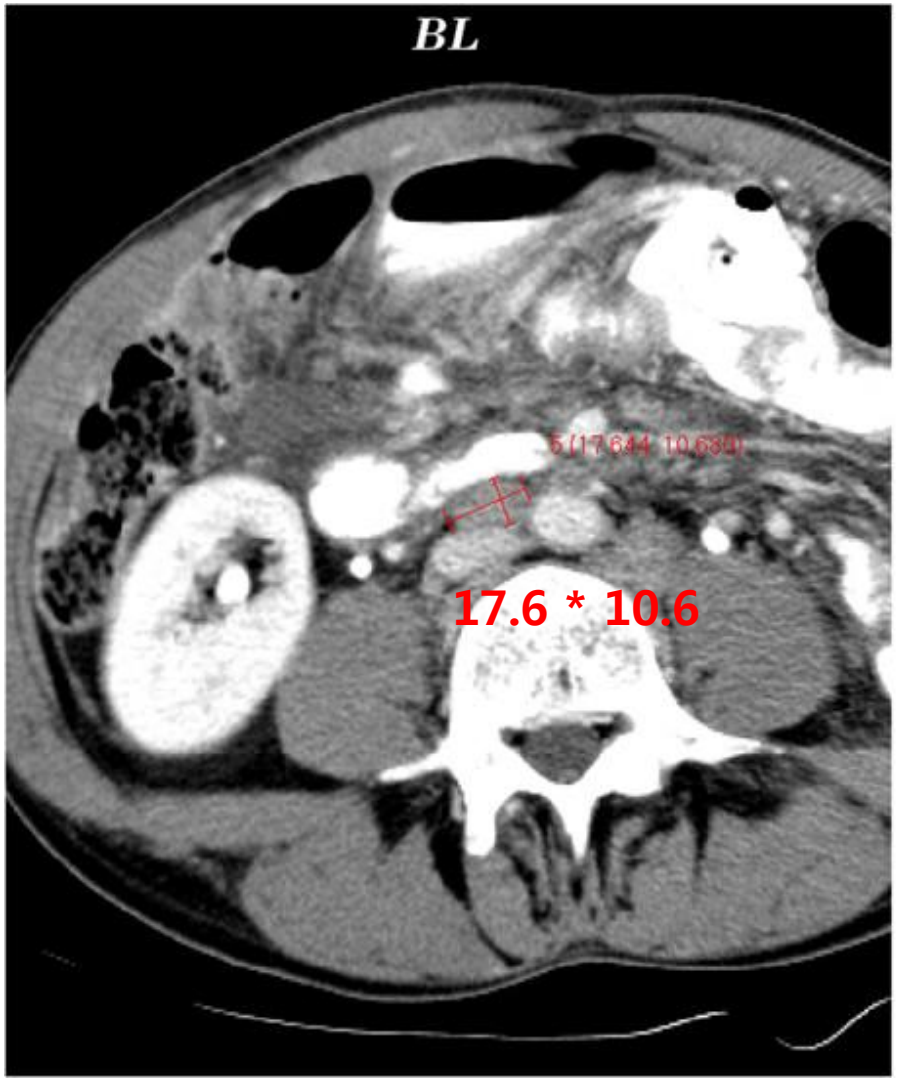
RECIST 1.1

- Definitions provided for
  - **Normal**: short axis < 10 mm
  - **Measurable (Target)**: short axis ≥ 15 mm
  - **Non-measurable**: short axis 10 to < 15 mm

- Target nodes measured in the **short axis** (perpendicular to longest diameter)

Lymph Node Measurements

- First, identify the longest diameter of a lymph node or nodal mass
- Then measure the longest perpendicular diameter to that as the short axis
- Long axis : 17.6 mm
  Short axis : 10.6 mm
  -> non-measurable



Baseline Documentation of Target Lesions

RECIST 1.0

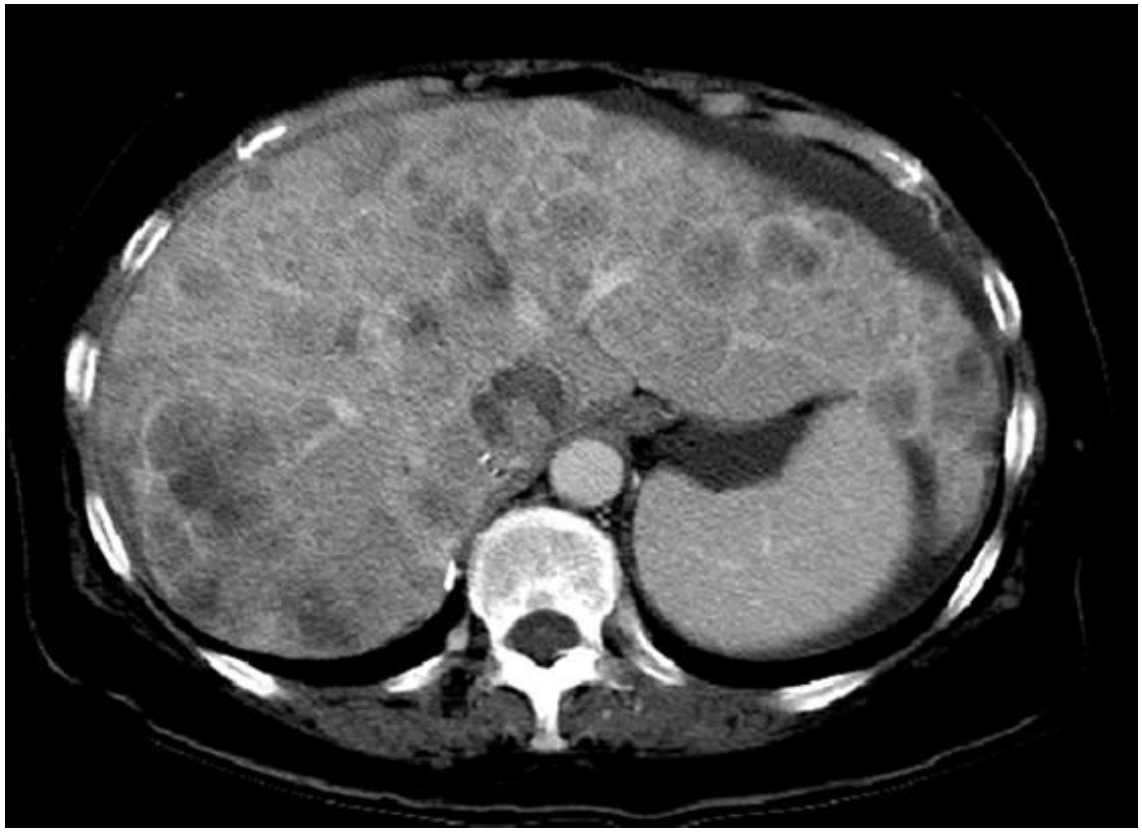
- All measurable lesions **up to 10 total (max of 5/organ)** Must be representative of all involved organs

RECIST 1.1

- All measurable lesions **up to 5 total (max of 2/organ)**
  - Must be representative of all involved organs
- **Selected on the basis of their size** and **suitability for accurate repeated measurements**
- **Short axis of target nodes to be added to the sum**

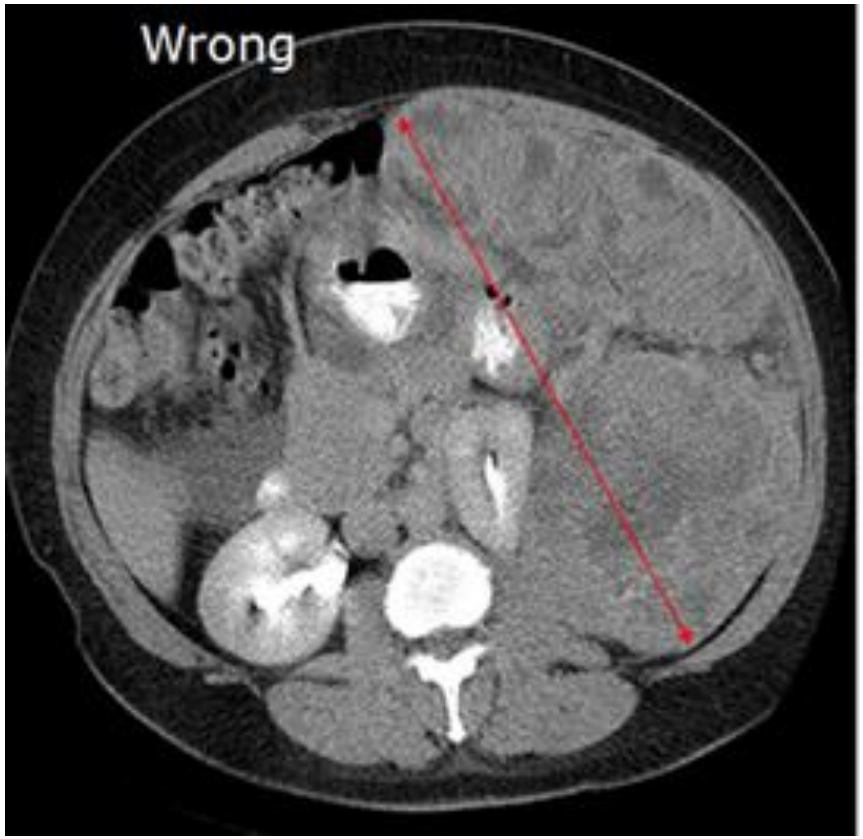
Selecting Target Lesions

- Do not necessarily select the largest lesions as target
- Select those that are best defined and reproducibly measurable



Target Measurement Rules

– Do not measure lesions across normal, non-tumor tissue



Documentation of Non-target Lesions

RECIST 1.0

- **All other lesions** (or sites of disease) should be identified as non-target lesions

- Measurements of these lesions are not required, but the presence or absence of each should be noted

RECIST 1.1

- **Measurement of the lesions is not required**
  - **Present or Absent**

- **Can record multiple non-target lesions in same organ as single item**
  - (e.g. "multiple enlarged pelvic lymph nodes" or "multiple liver metastases")

Definition of Complete Response (CR)

RECIST 1.0

- Lymph nodes with respect to CR not addressed

RECIST 1.1

- Target Lesions
  - **Disappearance of all target lesions**
  - **Any pathological LN (whether target or non-target) must have reduction in short axis to <10 mm**
- Non-target Lesions
  - Disappearance of all non-target lesions
  - Normalization of tumor marker level

Definition of Progressive Disease (PD)

RECIST 1.0

- No absolute increase in size required

RECIST 1.1

- Target Lesions
  - > 20% increase from smallest sum of diameter recorded since treatment started (best response, nadir)
  - **Minimum 5 mm increase over the nadir**
- Non-target lesion
  - Appearance of one or more new lesions
  - Unequivocal progression of existing non-target lesions
  - Must be representative of overall disease status change, not single lesion increase

Too Small to Measure

RECIST 1.0

- No specific recommendations

RECIST 1.1

- **All target lesions (nodal and non-nodal) recorded at baseline should have their actual measurements recorded** at each subsequent evaluation, even when very small (e.g. 2 mm)

- If target lesions become faint on CT scan, report them as being ‘too small to measure’ and default value of 5 mm

Lesions that Split or Coalesce

RECIST 1.0

- No specific recommendations

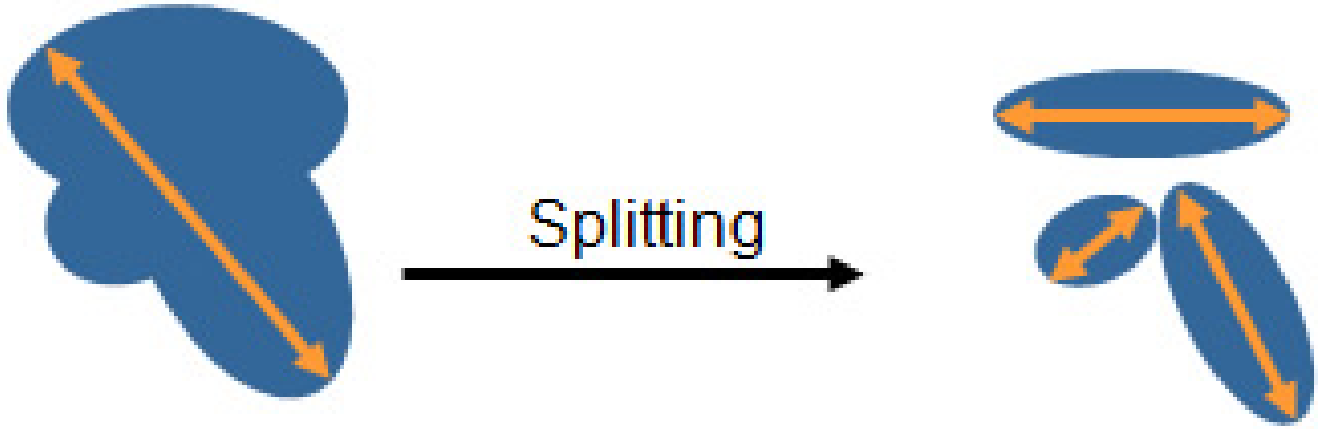
RECIST 1.1

- **If a target lesion separates, measure the longest diameter of each lesion separately**

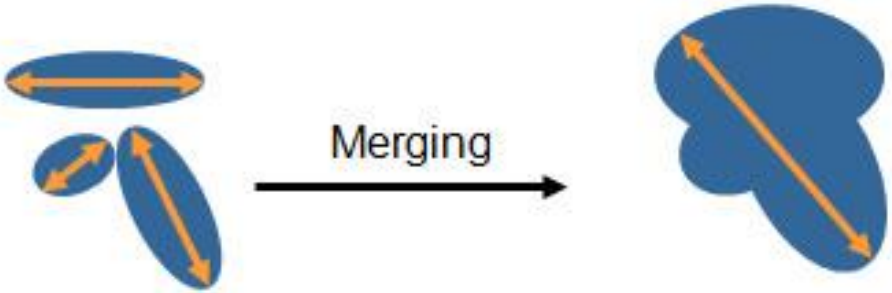
- If lesions have truly coalesced such that they are no longer separable, the vector of the longest diameter in this instance should be the maximal longest diameter for the 'coalesced lesion'

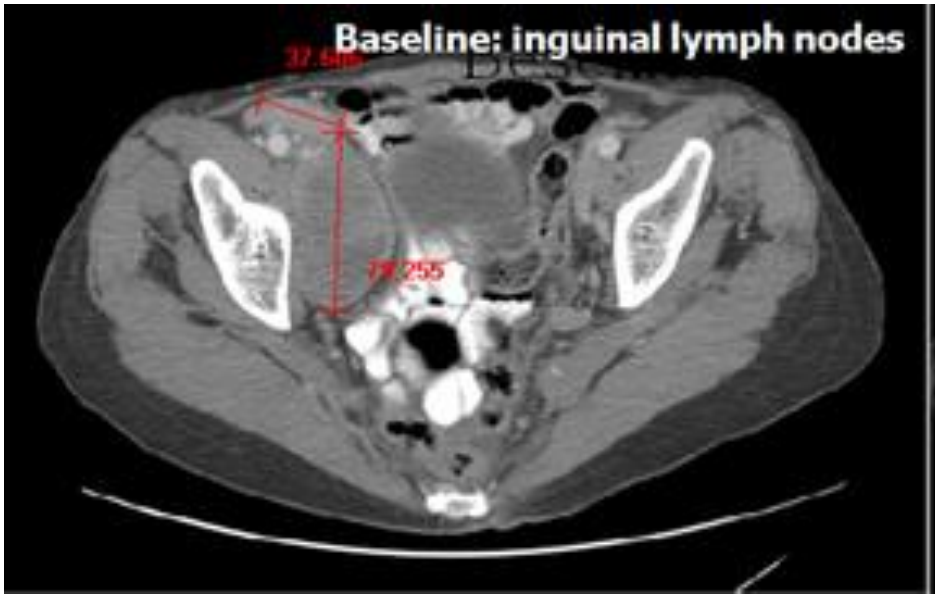
Splitting lesions

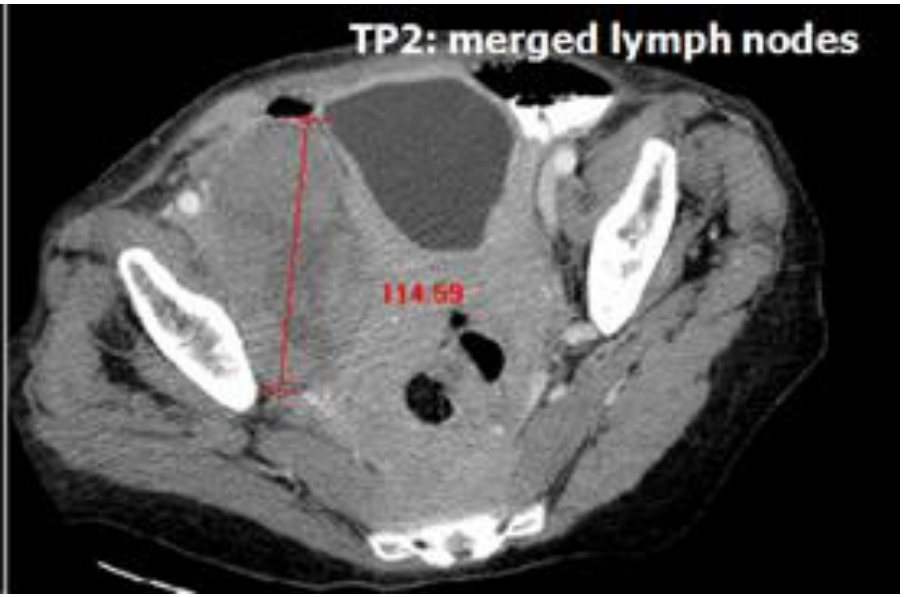
– The individual longest diameters of all the resulting lesions shall contribute to the sum of diameters



Merging Lesions







PET

RECIST 1.0

- No specific recommendations

RECIST 1.1

- Negative PET at baseline, with a positive PET at follow-up is PD based on a new lesion
- No PET at baseline and a positive PET at follow-up:
  - PD: corresponds to new site in CT
  - Equivocal: no new site on CT. additional follow-up CT scans are needed to determine if there is truly progression
  - Not PD: corresponds to pre-existing site on CT that is not progressing

Overall Response Table, Subjects with Measurable Disease

RECIST 1.0

Target	Non-target	New	Overall Response
CR	CR	No	CR
CR	IR/SD	No	PR
PR	Non-PD	No	PR
SD	Non-PD	No	SD
PD	Any	Yes or No	PD
Any	PD	Yes or No	PD
Any	Any	Yes	PD

RECIST 1.1

Target	Non-target	New	Overall Response
CR	CR	No	CR
CR	**Non-CR / non-PD**	No	PR
CR	**NE**	**No**	**PR**
PR	**Non-PD or NE**	No	PR
SD	**Non-PD or NE**	No	SD
Not all evaluated	**Non-PD**	**No**	**NE**
PD	Any	Yes or No	PD
Any	PD	Yes or No	PD
Any	Any	Yes	PD

Overall Response Table, Subjects without Measurable Disease

RECIST 1.0

- No specific recommendations

RECIST 1.1

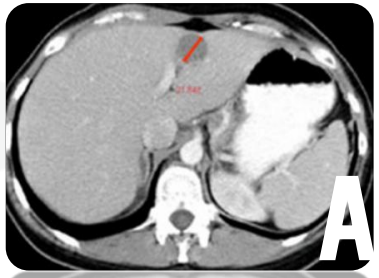
Non-target	New	Overall Response
CR	No	CR
Non-CR / non-PD	No	Non-CR / non-PD
Not all evaluated	No	NE
Unequivocal PD	Yes or No	PD
Any	Yes	PD

	RECIST 1.0	RECIST 1.1
Minimum Target Lesion Size	≥10 mm (Spiral CT) ≥20 mm (Conventional CT, MRI)	≥10 mm (CT + MRI) ≥15 mm Lymph nodes ≥20 mm Chest X-Ray
No. of measurable Lesions, per organ	1-10 5	1-5 2
Lymph node Measurements	None	Specific instructions ≥15mm, 10-14mm, <10mm
Measurement	Uni-Dimensional	Uni-Dimensional Lymph nodes = short axis
PD	20 % increase in SOD from Nadir	20 % increase in SOD + min. 5mm increase from Nadir
Confirmation of CR and PR	After at least 28 days	Only required, if response is primary endpoint and not randomized
Non Measurable Assessment	Unequivocal progression	Substantial worsening
PET	Not available	May be considered to support CT

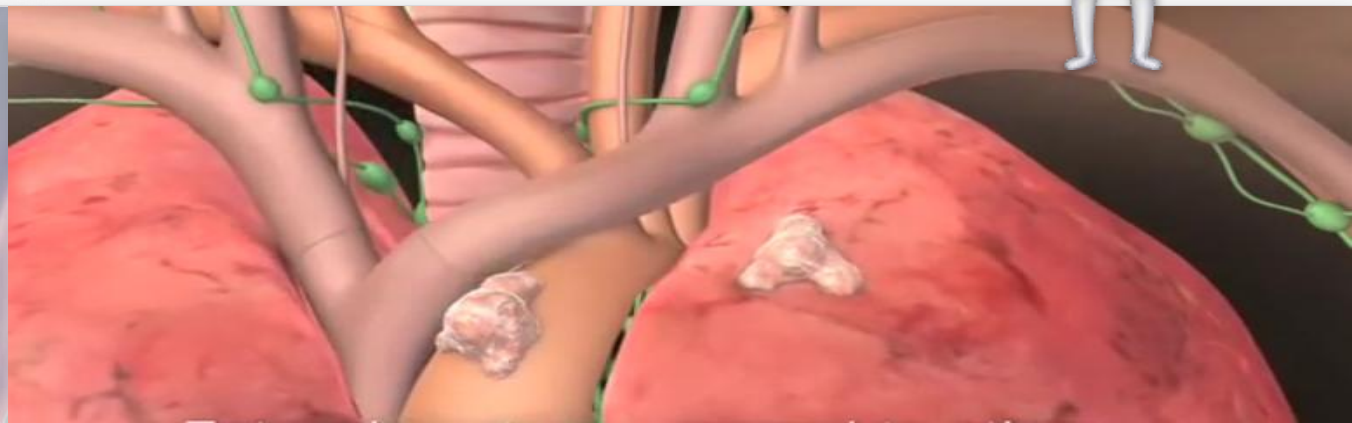
http://www.irrecist.com/recist/recist-comparative


지루하다


졸지 말고 눈 뜹니다.
문제는 풀어야 제 맛이지 말입니다.!



Applying the Rules



CASE 1 : Definition of Baseline/Nadir as Reference

Lesion	BL	#1
Rt. Lung #1	3	2
Rt. Lung #2	2.5	2
Lt. liver lobe	6	5
Hilar LN	2.5	2
Total Length	14	11
% Change		-21%
Disease Status		SD

- Longest diameter of tumor lesion & short axis diameter of LN (cm)
- 11/14 = 0.79 : -21%
- Not 30% decrease
  = SD

CASE 1 : Definition of Baseline/Nadir as Reference

Lesion	BL	#1	#2
Rt. Lung #1	3	2	2
Rt. Lung #2	2.5	2	2
Lt. liver lobe	6	5	3
Hilar LN	2.5	2	2
Total Length	14	11	9
% Change		-21%	-36%
Disease Status		SD	PR

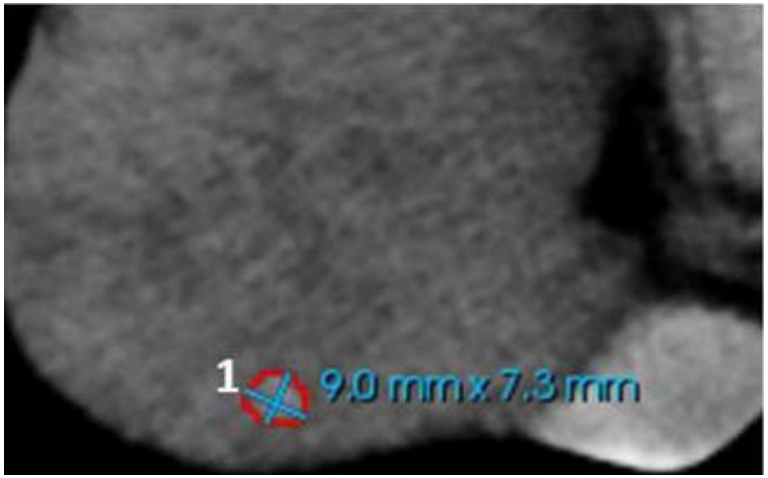
- 9/14 = 0.64 : -36%
- >30% decrease = PR

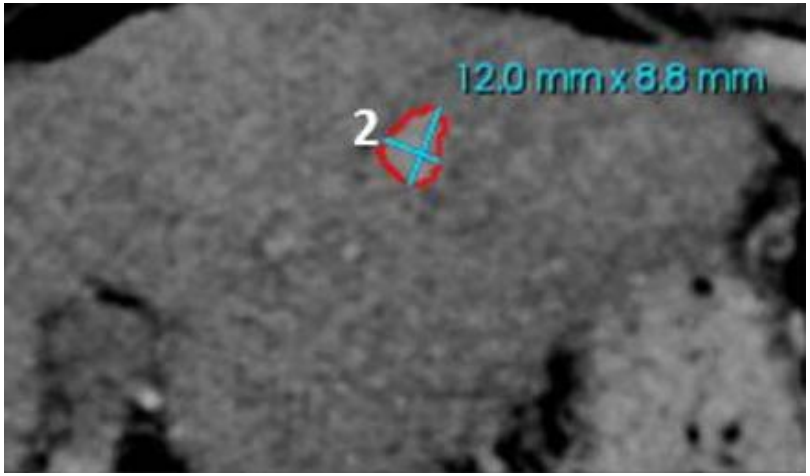
CASE 1 : Definition of Baseline/Nadir as Reference

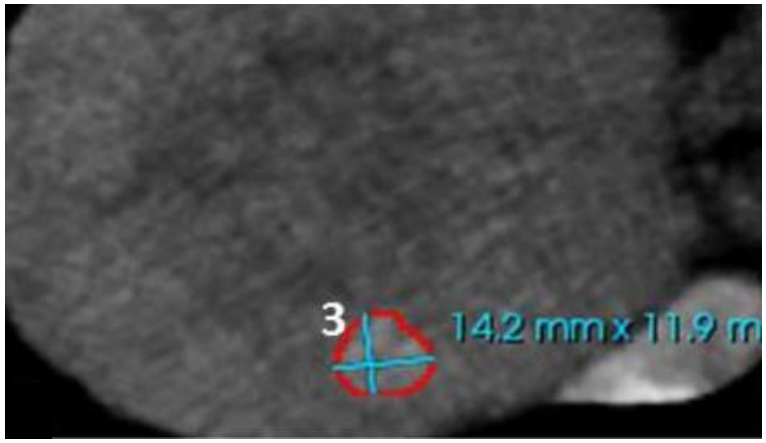
Lesion	BL	#1	#2	#3
Rt. Lung #1	3	2	2	3
Rt. Lung #2	2.5	2	2	4
Lt. liver lobe	6	5	3	6
Hilar LN	2.5	2	2	3
Total Length	14	11	9	16
% Change		-21%	-36%	+77%
Disease Status		SD	PR	PD

- Change from nadir
- 16/9 = 1.77
  : 77%
- PD >20%, increase from nadir

CASE 2 : Assignment of Non-qualifying Target Lesions (Number & Size)

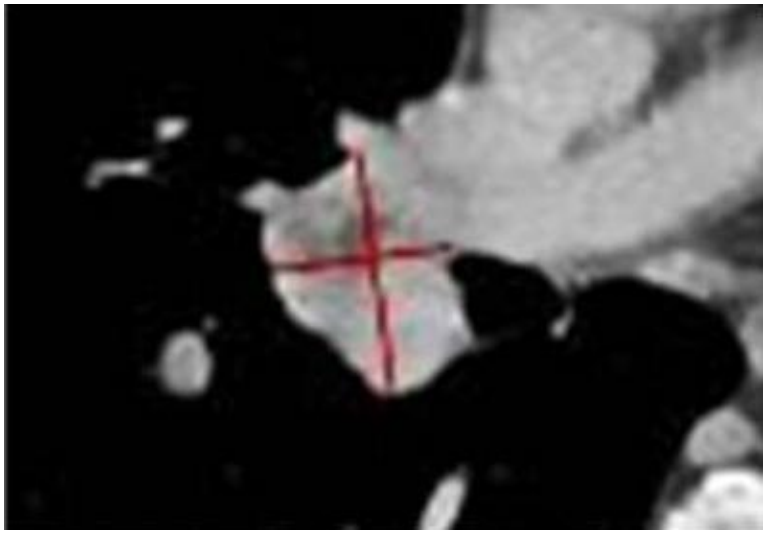


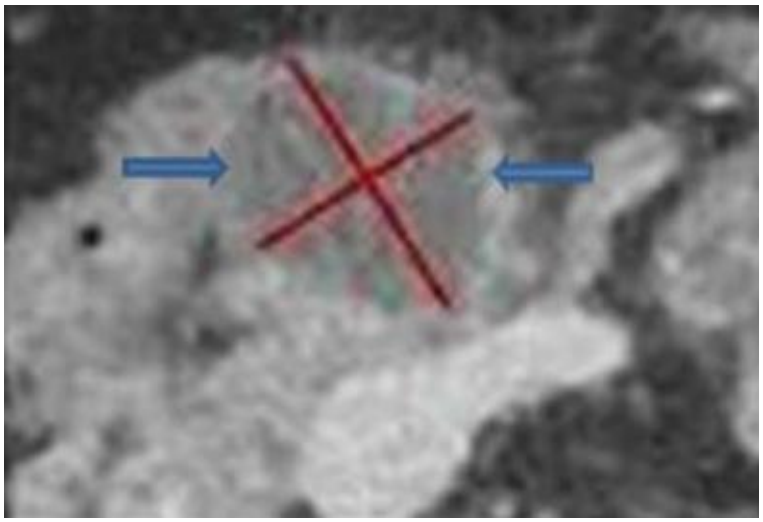




- Three liver metastases are assigned as target lesions instead of two
- 1st lesion does not fulfill criteria

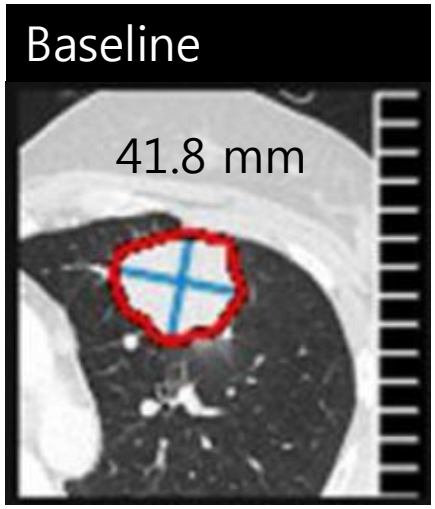
CASE 3 : Assignment of Non-qualifying Target Lesions (Pseudolesion)

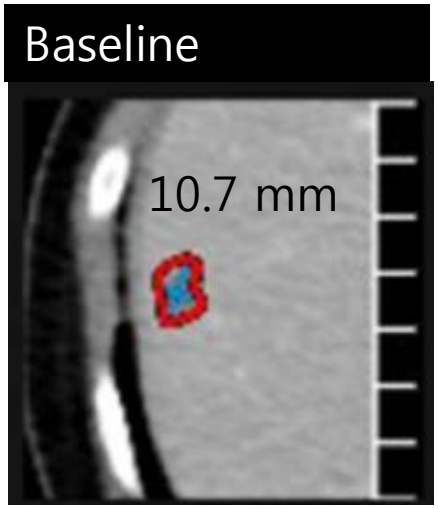


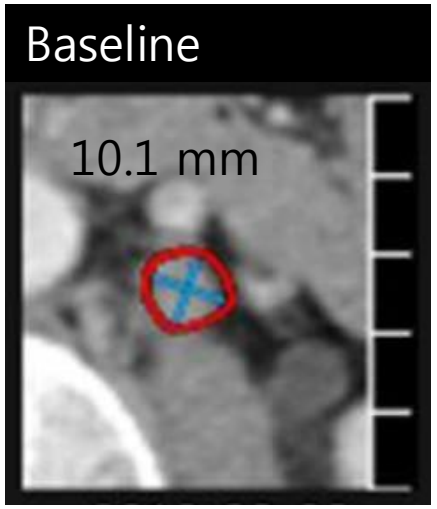


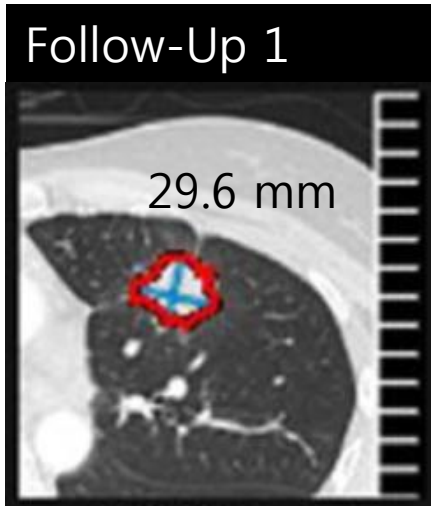
- Two lung lesion and one cystic lesion in pancreas
- f/u examinations proved this cystic pancreas lesion to be IPMN

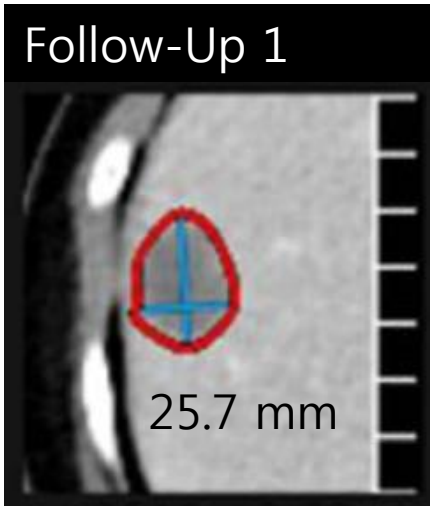
CASE 4 : Miscalculation of Mixed Response





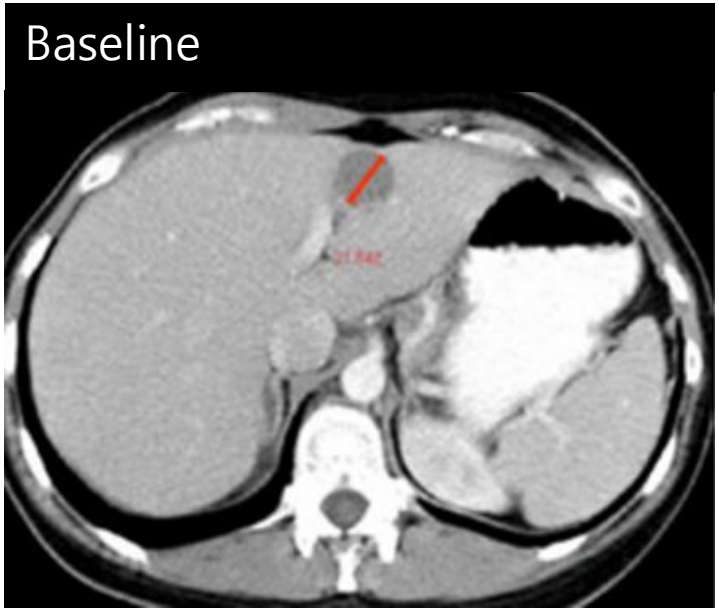


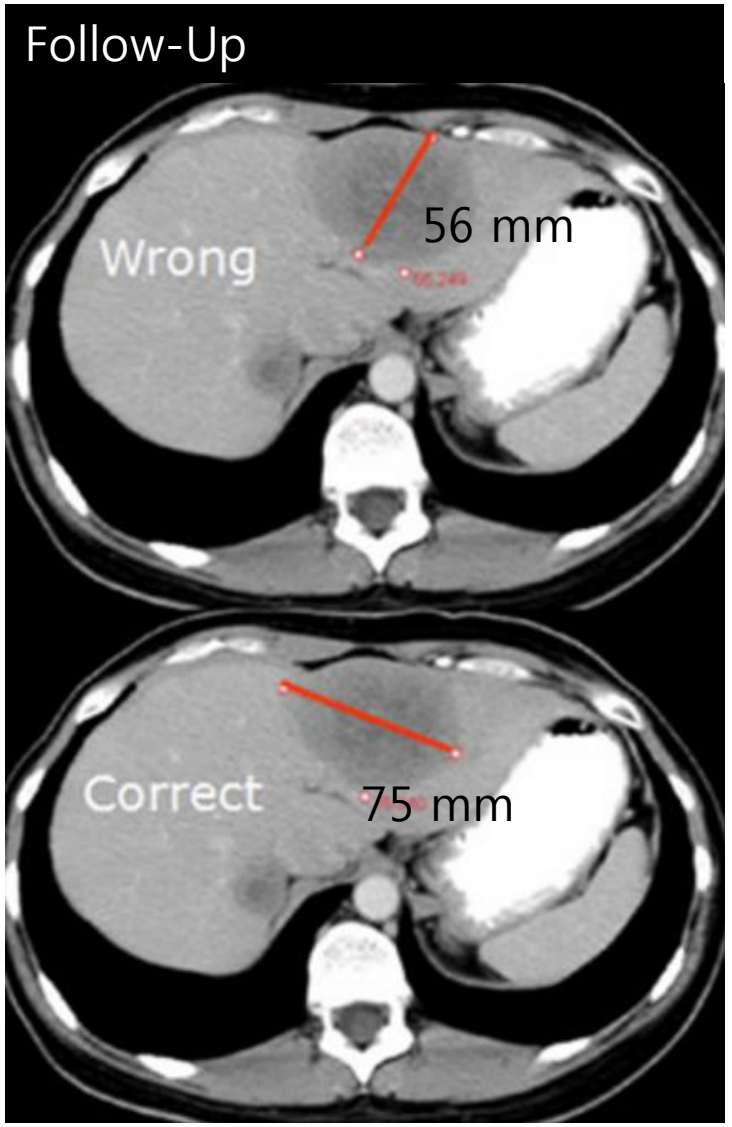


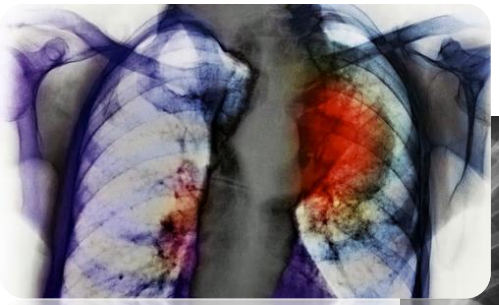


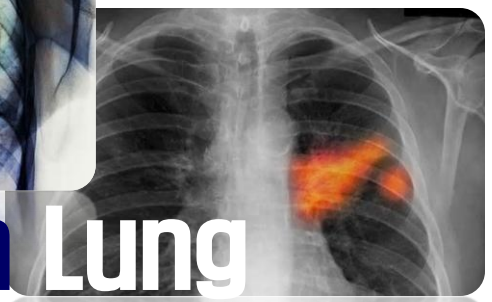
- Lung lesion show PR
- But, all are suggestive PD
- 76.3 / 62.6 = 1.21 : +21%

CASE 5 : Miscalculation of Target Measurement

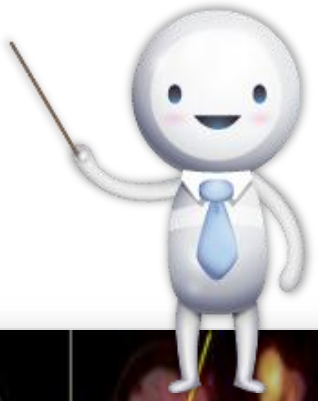


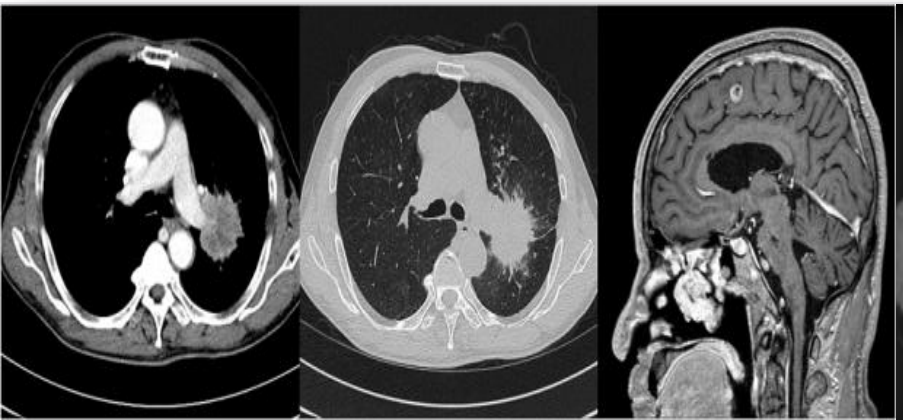


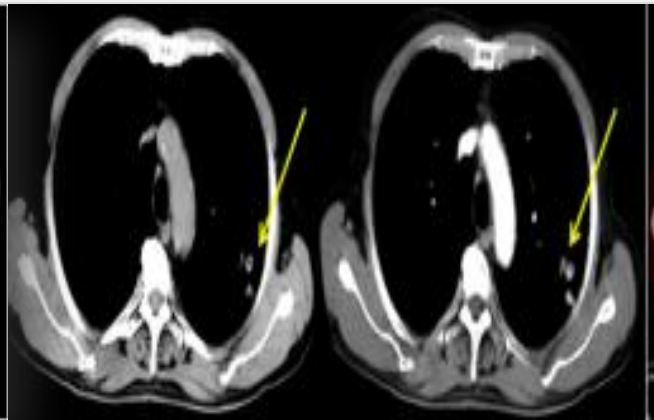


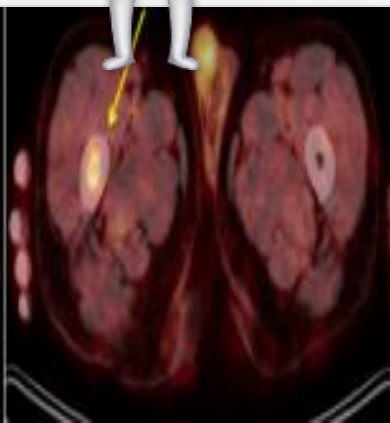


Special Considerations in Lung Cancer

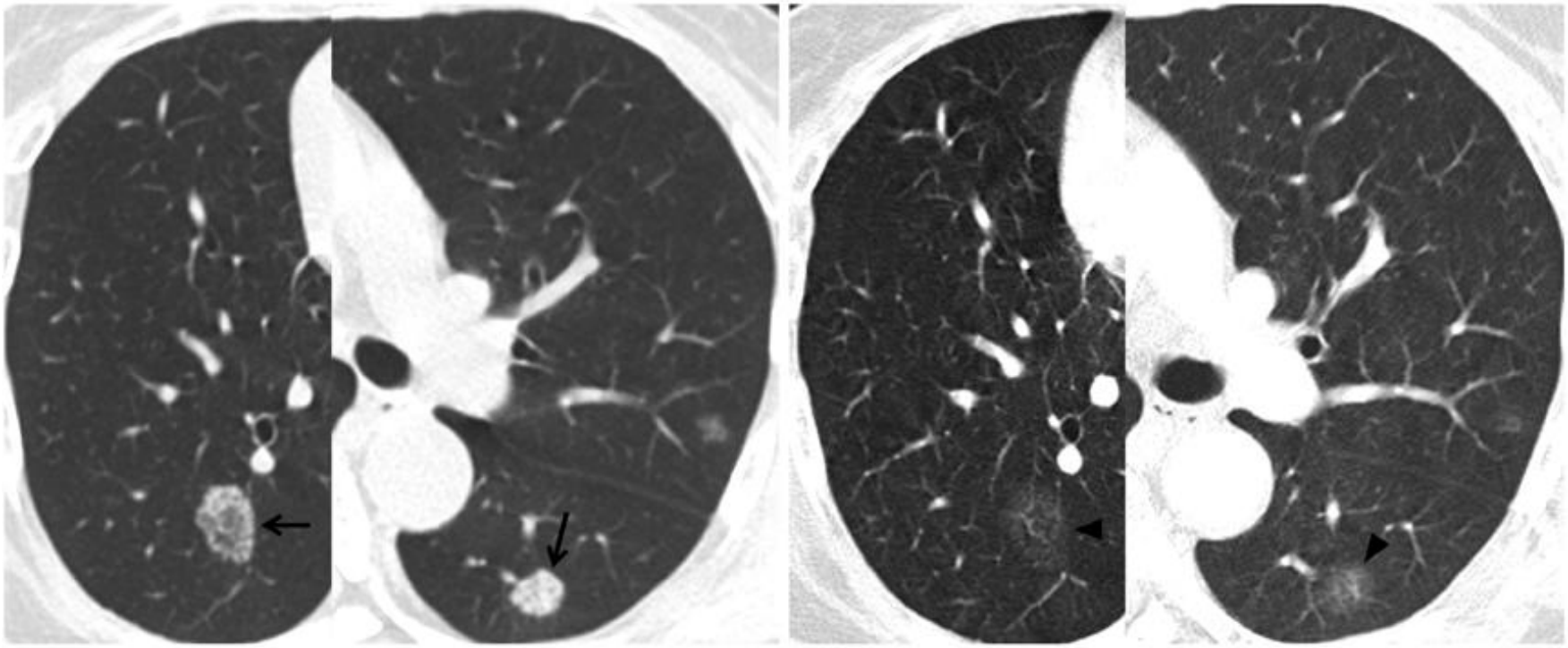








GGO Lesion and Part-solid Nodule



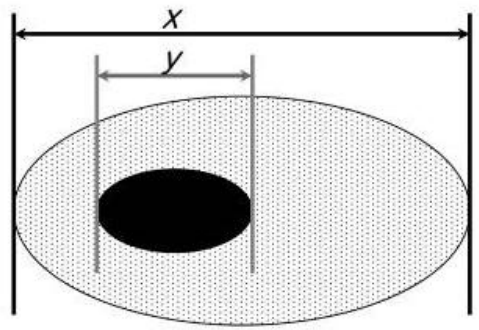
Patient with EGFR+ lung adenocarcinoma (Exon 19 microdeletion) 2 cycle of gene target therapy with Gefitinib

Only GGO components of lesion remain without significant change of diameter

GGO Lesion and Part-solid Nodule

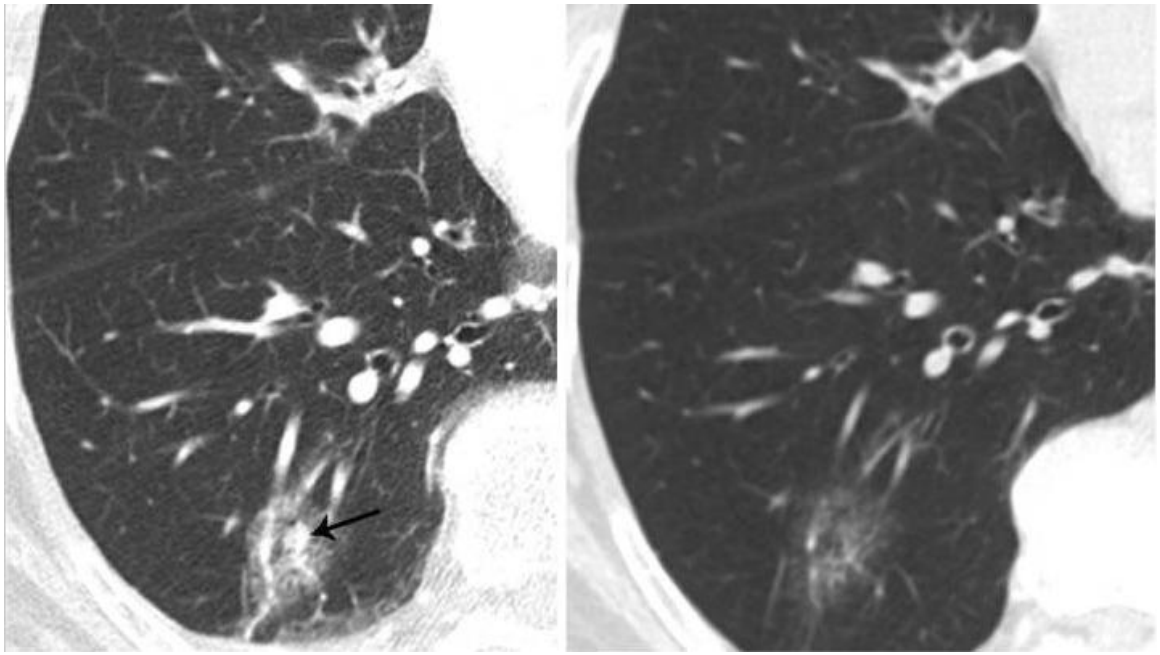
- Lung cancer is generally measured on lung window and include both GGO areas and solid components in part-solid lung cancer
- However, GGO within part-solid lung cancer generally does not vary profoundly with cancer chemotherapy
- Size change in only solid component of part-solid peripheral lung cancer may be more accurate reflection of the actual tumor response to cancer chemotherapy

GGO Lesion and Part-solid Nodule



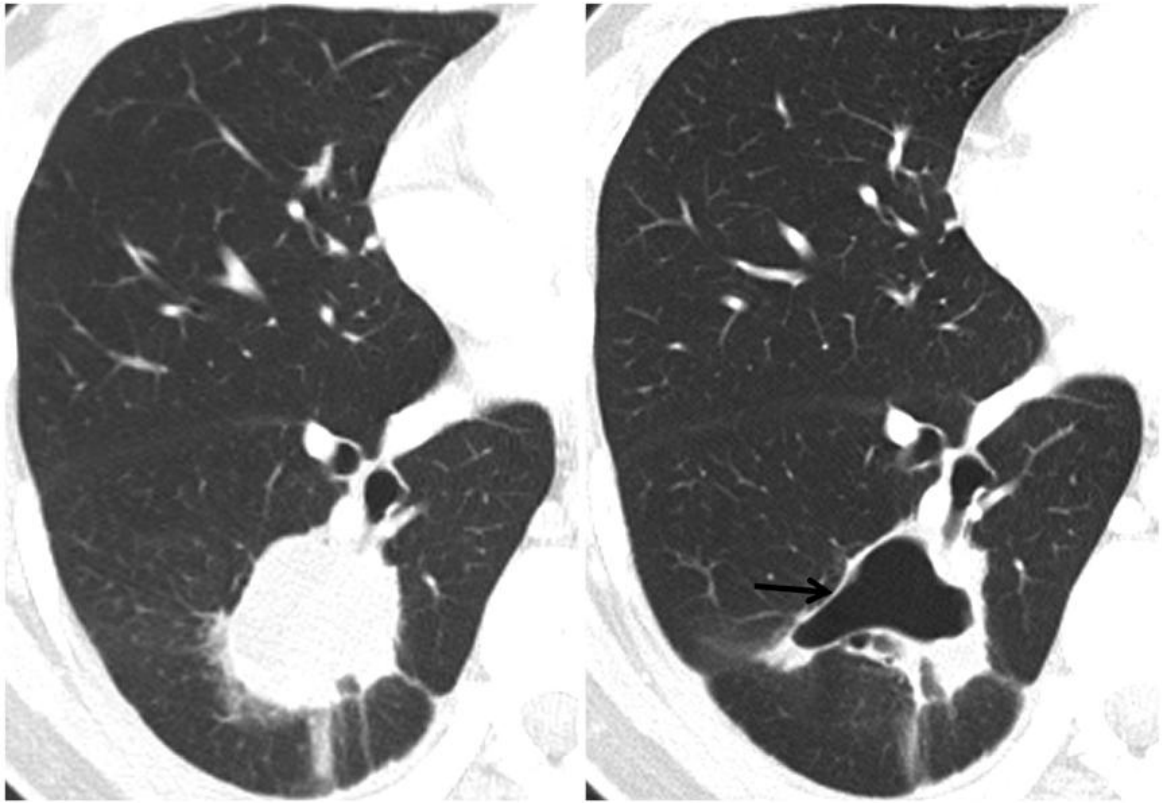
RECIST measurement = *x*

RECISTsolid measurement = *y*



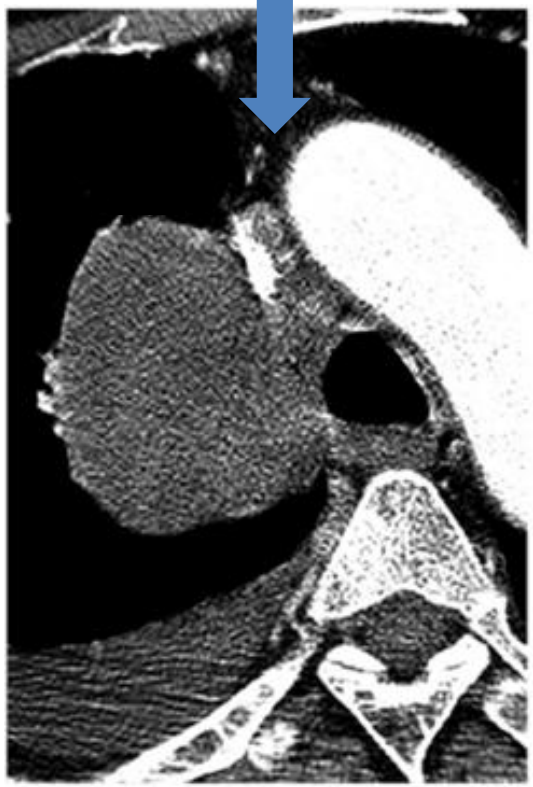
Lee et al. Lung Cancer 2011

Cavitation Lesion

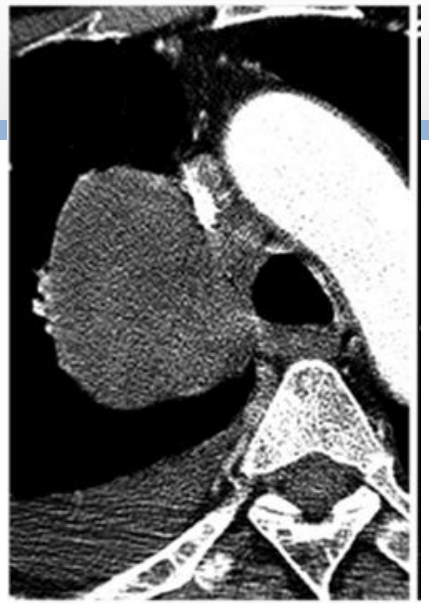


Patient with NSCLC

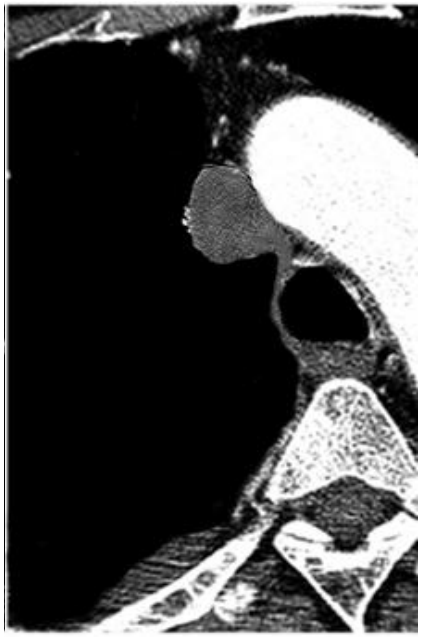
Lung image after chemotherapy show internal cavity formation due to necrosis of tumor



Response



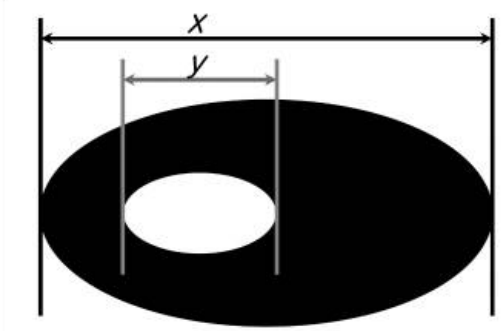
Non-Response



Cavitation Lesion

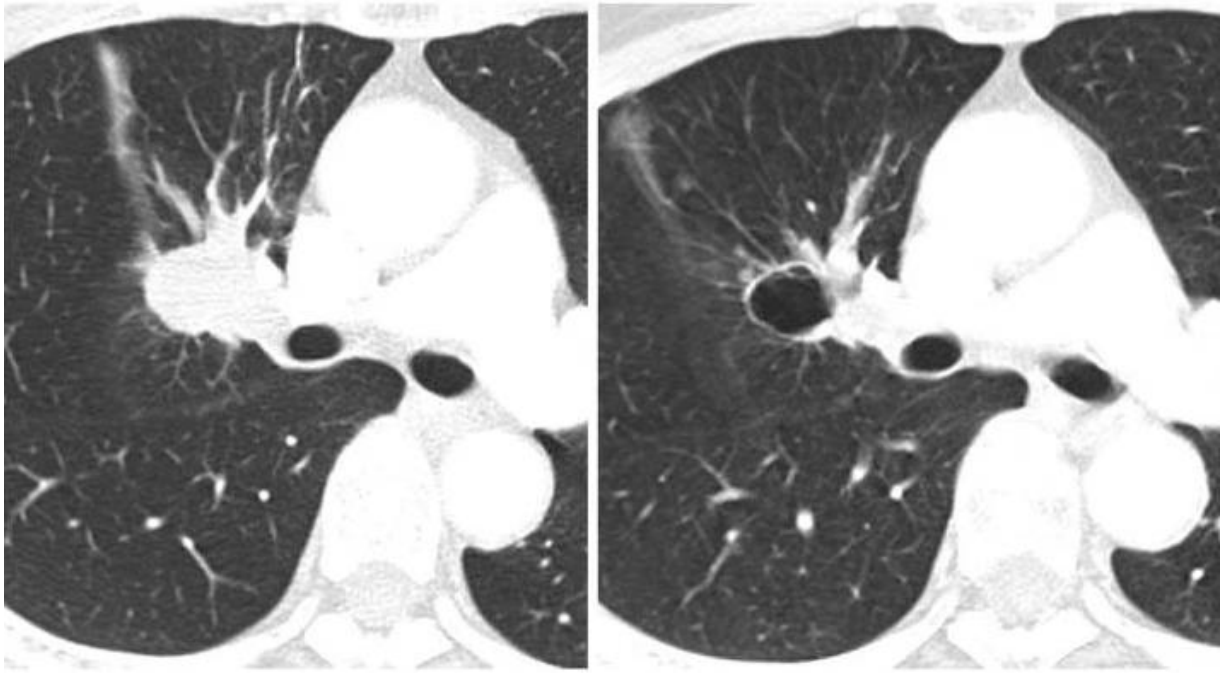
- Cavitation within a tumor caused by hampered angiogenesis
  - Specially, in NSCLC, treated with vascular endothelial growth factor (VEGF) receptor inhibitor and platinum-based chemotherapy
- Tumor necrosis may constitute a type of tumor response, but RECIST focus on tumor size only

Cavitation Lesion



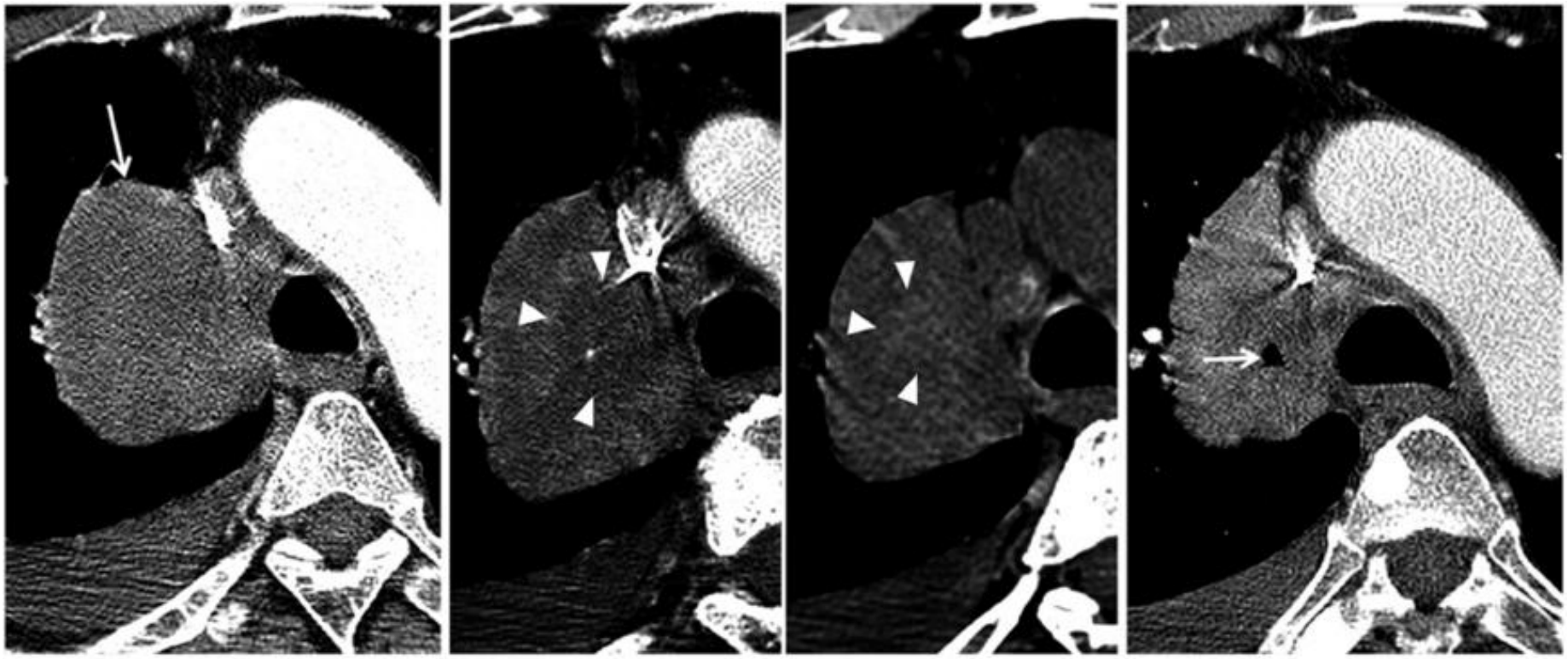
RECIST measurement = x

Alternative measurement = $x - y$



Lee et al. Lung Cancer 2011

Attenuation Change



#1, CT show no diameter change, but, heterogeneously decreased attenuation within tumor on contrast CT. And increased attenuation on non-contrast CT, suggesting internal hemorrhage.

#2, Mass has shrunk and internal cavity formation, suggesting tumor necrosis

Attenuation Change

Choi Response Criteria

Response	Definition
CR	Disappearance of all lesion No new lesion
PR	Decrease in size ≥10% or decrease in tumor attenuation (HU) ≥15% on CT No new lesion No obvious progression of non-measurable disease
SD	Does not meet criteria for CR, PR or PD No symptomatic deterioration attributed to tumor progression
PD	Increase in tumor size ≥ 10% and does not meet criteria of PR by tumor attenuation on CT New intratumoral nodules or increase in the size of the existing intratumoral nodules New lesion

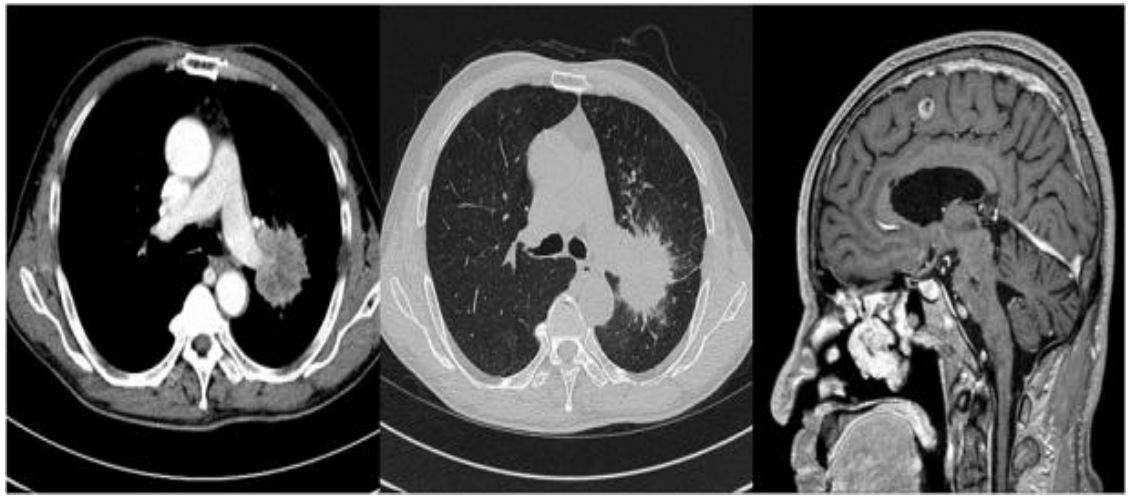
Choi et al. J Clin Oncol 2007

CT Morphologic Features of Pulmonary Adenocarcinoma with Brain/bone Metastasis

- **Variables predictive of brain metastasis on multivariate analysis**

	Odds ratio	95% Confidence Interval	*p*-value
Size			
≥ 50mm	3.37	1.24-9.17	< 0.05
Necrosis			
≥ 30 %	4.51	1.62-12.55	< 0.05
Calcification			
present	3.97	1.16-13.55	0.073

- **뇌전이 폐암환자의 CT 방사선학적 특징분석 (좌: Necrosis, 우: Spiculation)**

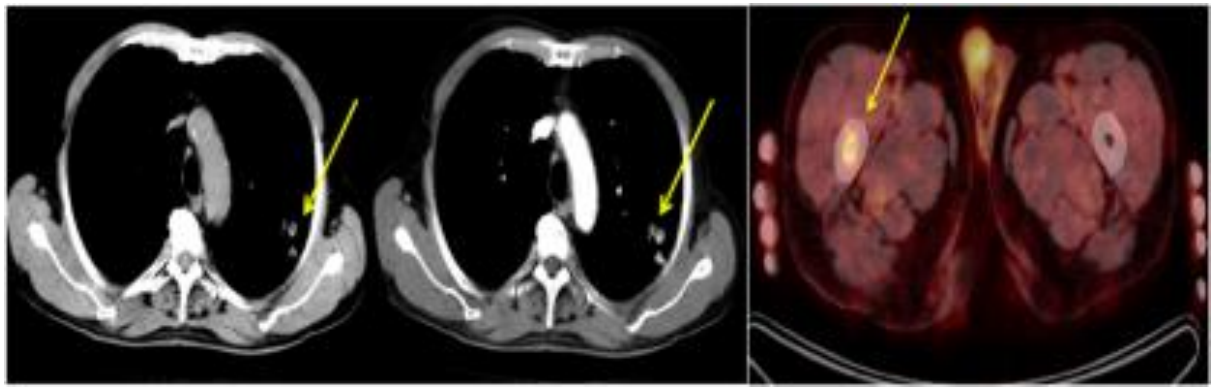


CT Morphologic Features of Pulmonary Adenocarcinoma with Brain/bone Metastasis

- **Variables predictive of bone metastasis on multivariate analysis**

	Odds ratio	95% Confidence Interval	*p*-value
Size			
≥ 50mm	2.05	0.88-4.77	0.78
Necrosis			
≥ 30 %	4.69	1.98-10.82	< 0.05
Calcification			
present	1.23	0.35-4.23	0.97
T stage			
T3-4	2.53	1.07-6.00	< 0.05

- **폐암환자의 CT 방사선학적 소견 (Lobulated calcification, Air cavity 소견 및 우측 대퇴골전이의 PET-CT 소견**

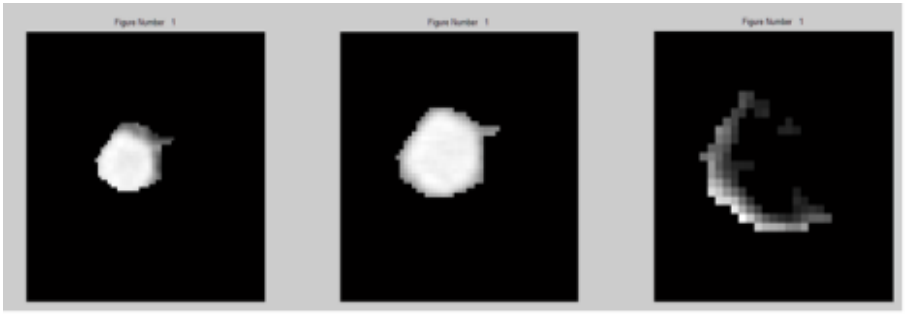



소고기 등급 기준표
1++등급
1+등급
1등급
2등급
3등급


등급은
내 맘대로~
Objective(Bias)

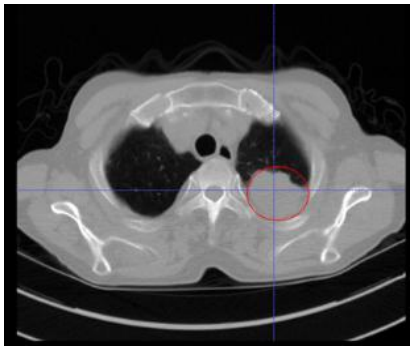
폐 질환 CT 분석 알고리즘 개발

- 폐 질환 예상인자에 대한 괴사 세포 획득 영상

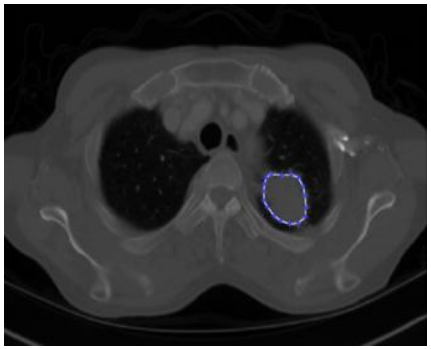


〈 moving image〉 〈 fixed image〉 〈 괴사 세포 image〉

- 폐 질환의 영상



- 질병 부분 분할

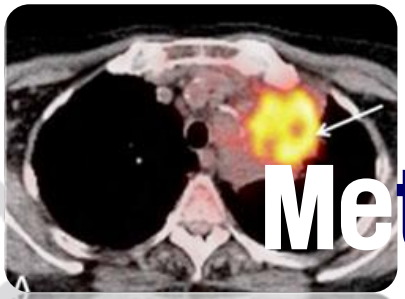


- 12명 환자에 대한 수치화 결과

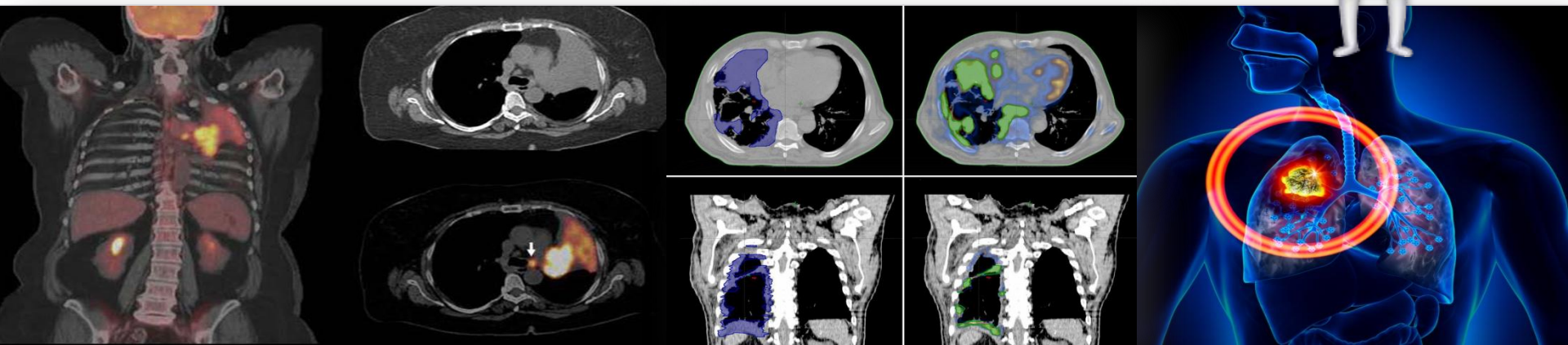
환자(수)	괴사 세포 비율(%)	살아 있는 세포 비율(%)
1	16.7	83.3
2	68.8	31.2
3	56.6	43.4
4	92.1	7.9
5	59.6	40.4
6	35.6	64.4
7	44.2	55.8
8	70.6	29.4
9	85.5	14.5
10	84.5	15.5
11	80.6	19.4
12	47.8	52.2

특허등록

의료 영상 분석 장치 및 이의 폐결절과 폐혈관 구분 방법
2016.01.15, 등록번호 10-1587719



Metabolic, Functional, and Nonanatomical Imaging Technique



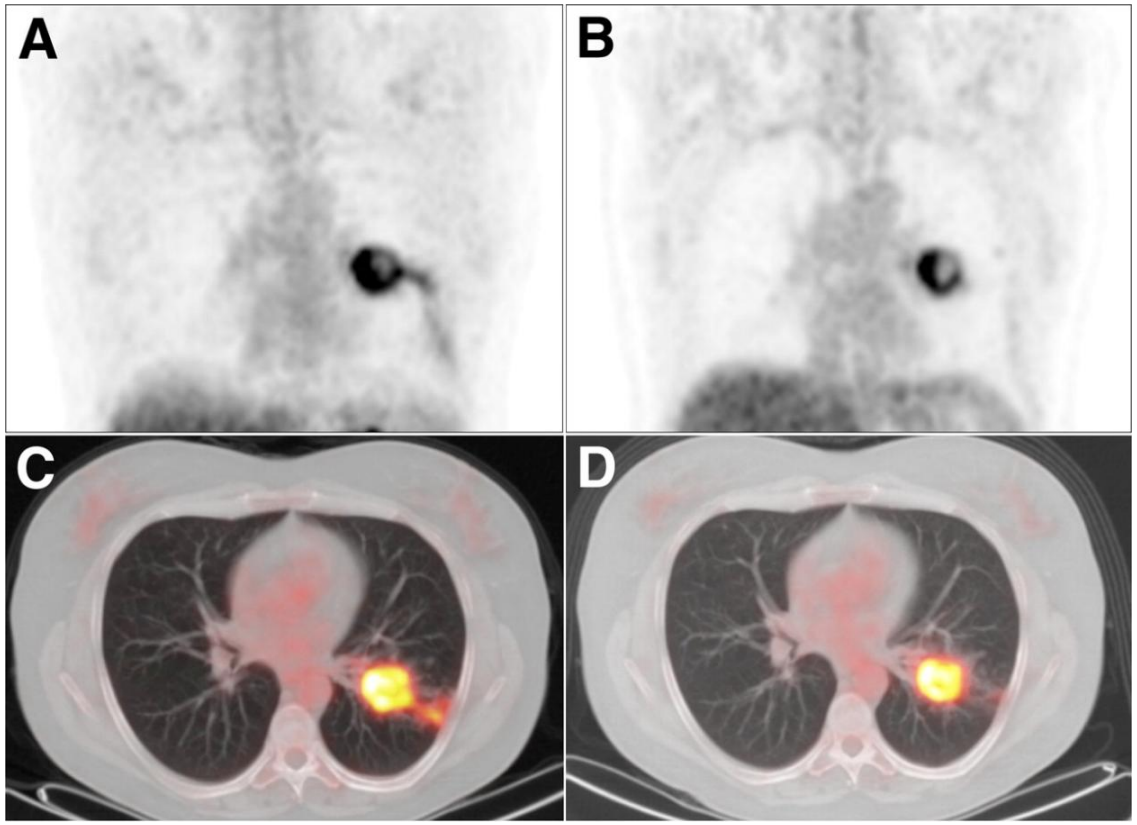
^{18}F–FDG PET

- In NSCLC,
  - Adequate staging tool
  - Related to prognostic value in several study
  - Predict response early during chemotherapy and target therapy

Berghmans T et al. J Thorac Oncol 2008

Lee DH et al. J Thorac Oncol 2009

^{18}F–FDG PET



- NSCLC, Tx with erlotinib
- A -> B
  - Increase in necrosis of primary tumor after 7 d
- C -> D
  - reduction in uptake (ΔSUV_{max}, −57%),
- After erlotinib treatment, patient was operated on; resected specimen contained 80% necrosis.

Aukema TS et al. J Nucl Med 2010

PET Response Criteria in Solid Tumor (PERCIST)

Role of FDG PET/CT in assessing response to targeted therapy in metastatic lung cancers: Morphological versus metabolic criteria.

Puranik AD[1], Purandare NC[1], Shah S[1], Agrawal A[1], Rangarajan V[1].

⊕ **Author information**

Abstract

INTRODUCTION: Targeted therapeutic agents are indicated in metastatic lung cancers. These being receptor specific therapies, manifestation of response can be best assessed by estimating the metabolic activity of tumor, rather than the size. This retrospective analysis studied metabolic and morphological response on Positron Emission Tomography (PET) and Computed Tomography (CT), respectively to these agents.

MATERIALS AND METHODS: Thirty-one patients (23 males, 8 females with an age range of 42-77 years) with Epidermal Growth Factor Receptor (EGFR) positive metastatic lung cancer on Gefitinib, who underwent PET/CT, at baseline and at 4-6 weeks, were assessed by Response Evaluation Criteria In Solid Tumors [RECIST] 1.1 and European Organization for Research and Treatment of Cancer (EORTC) criteria.

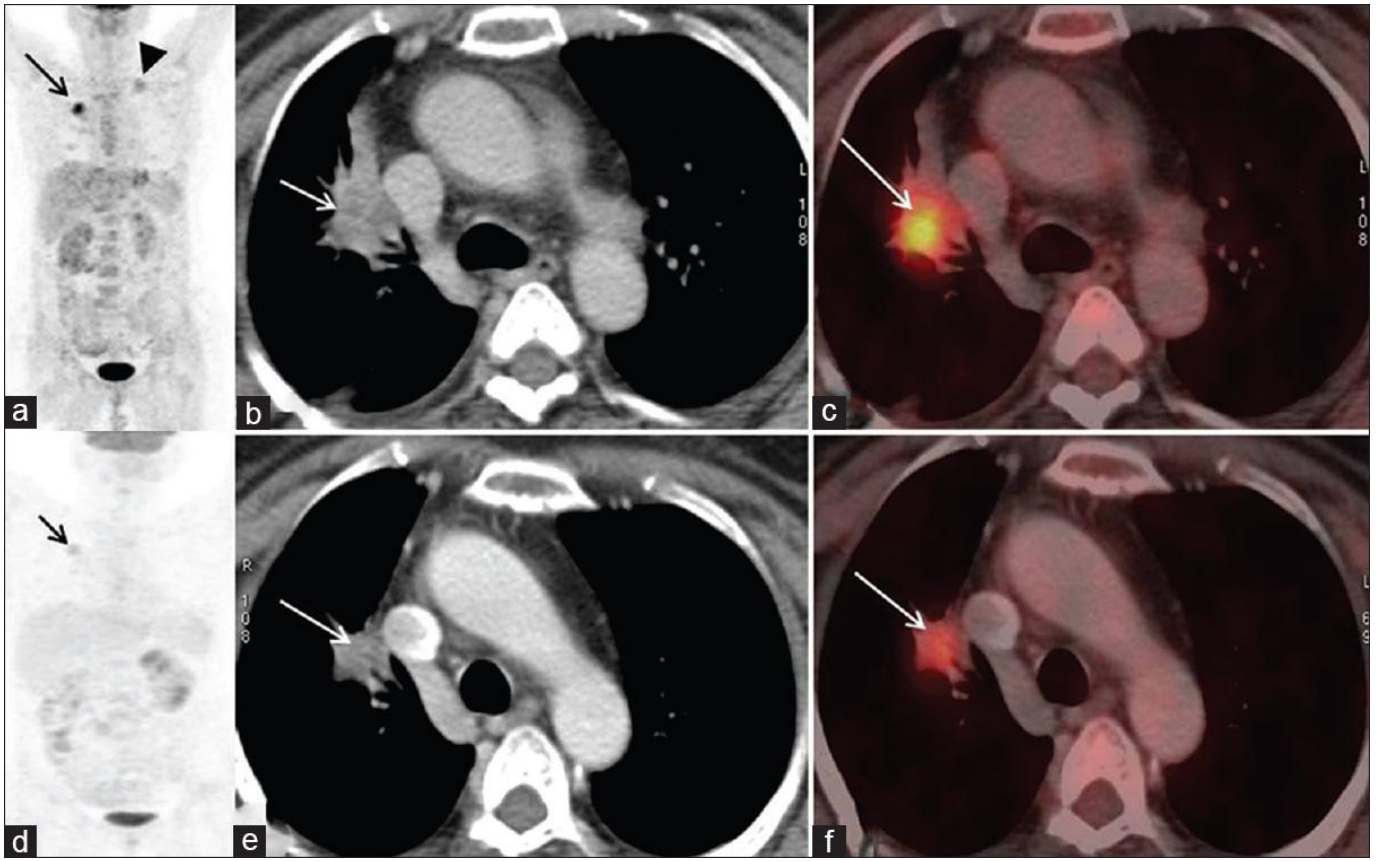
RESULTS: Concordance between RECIST 1.1 and EORTC was seen in 26 (83.7%) patients. Discordance was seen in 5 (16.3%) patients. In patients with discordance, the results were confirmed by follow-up imaging. Metabolic EORTC criteria changed the disease status from stable disease to partial response (3 out of 5) and progressive disease (2 out of 5) in these five patients.

CONCLUSIONS: Metabolic criteria using PET/CT could accurately predict response as well as disease progression early in the course of targeted therapy, compared to morphologic criteria. In addition, early metabolic response assessment can predict refractoriness of therapy.

KEYWORDS: Computed Tomography; Epidermal growth factor receptor; European organization for research and treatment of cancer; Fluoro-deoxy glucose positron emission tomography; Gefitinib; Lung cancer; Response; Response evaluation criteria in solid tumors

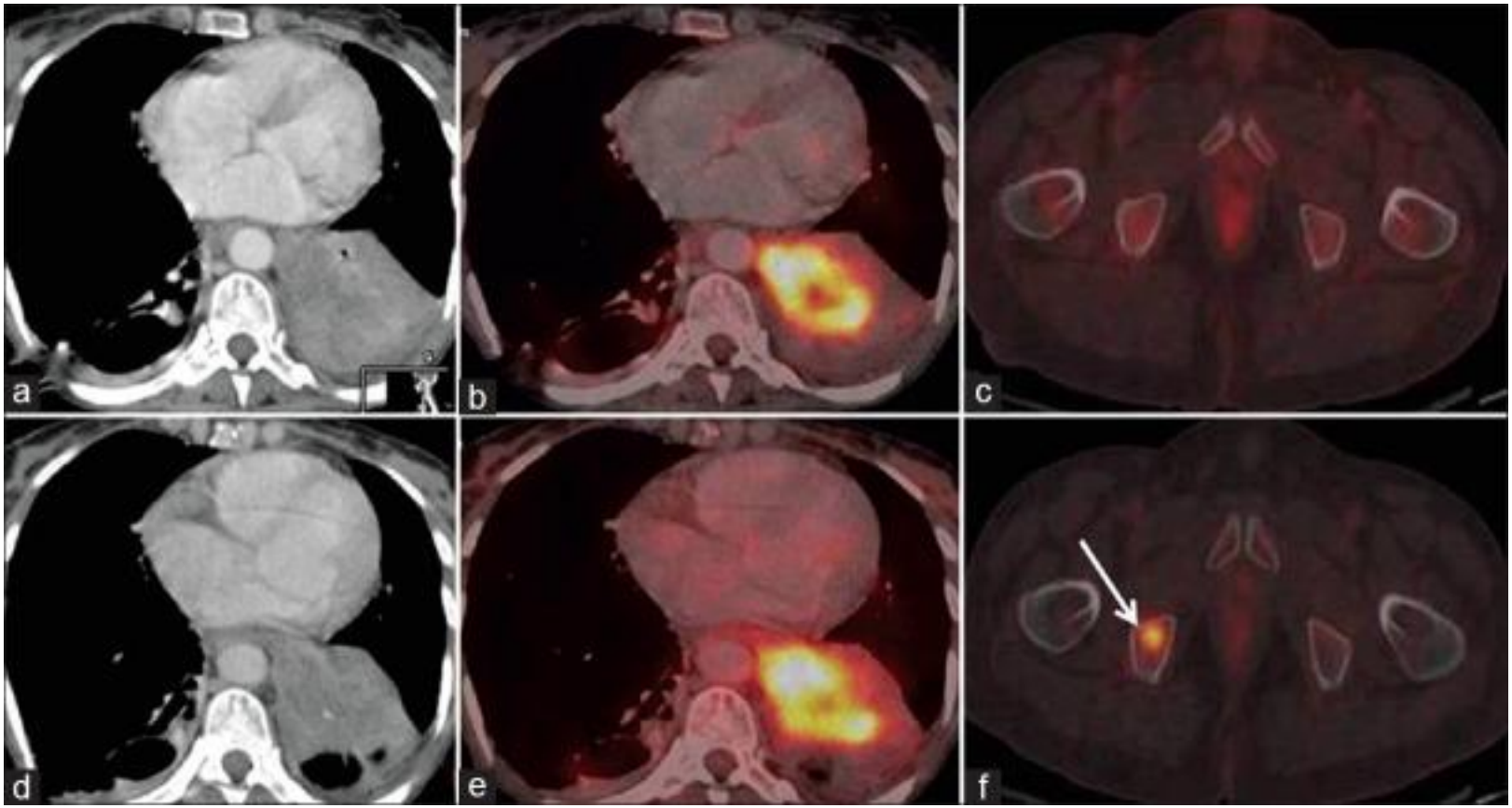
Indian J Nucl Med. 2015

PET Response Criteria in Solid Tumor (PERCIST)



Indian J Nucl Med. 2015 Jan-Mar;30(1):21-5.

PET Response Criteria in Solid Tumor (PERCIST)



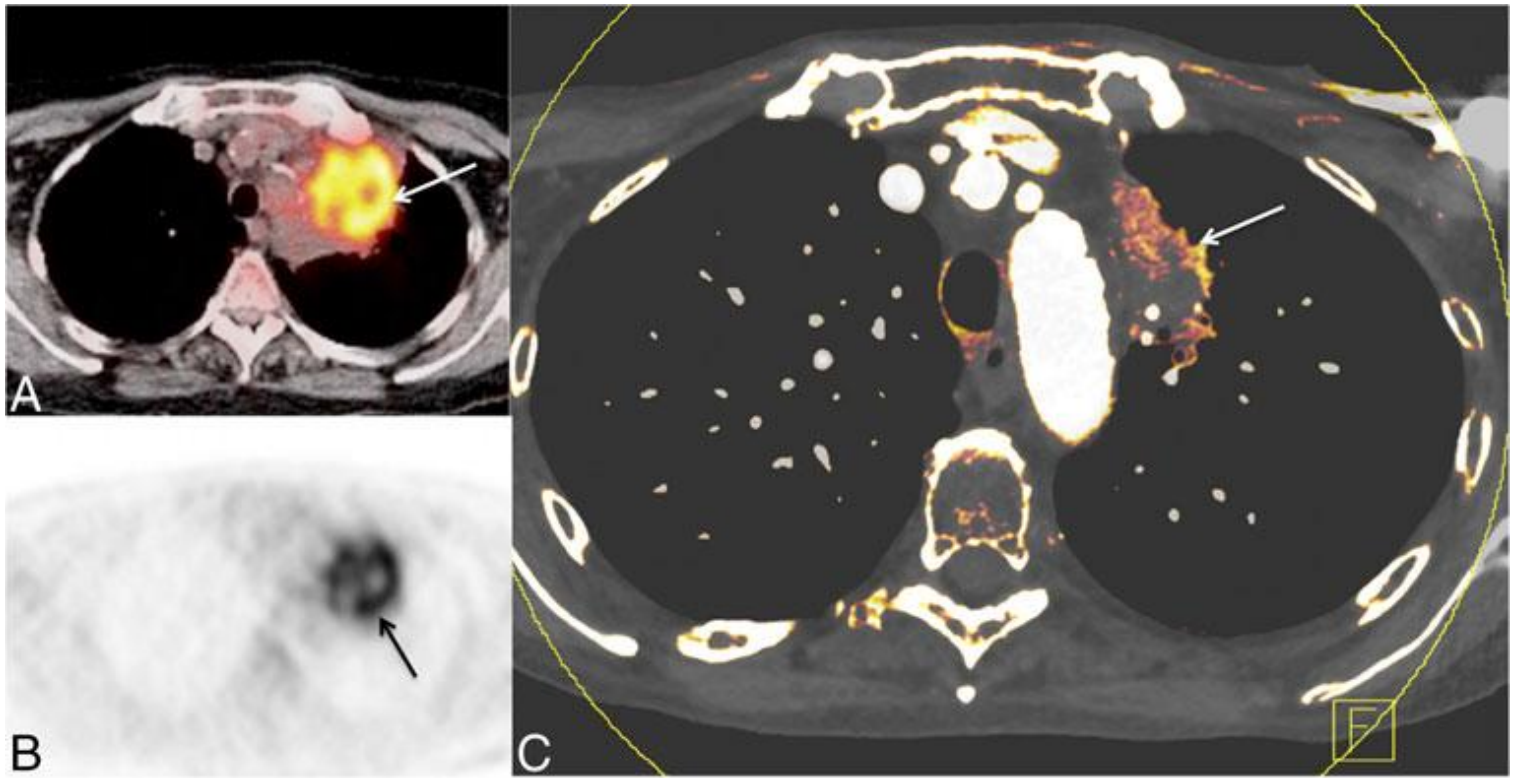
Indian J Nucl Med. 2015 Jan-Mar;30(1):21-5.

Dual-Energy CT (DECT)

- Useful functional imaging test for NSCLC
  - Enables selective visualization and quantification of the iodine-related attenuation (IRA) of intravenously injected iodinated contrast material
  - Provides information on tumor angiogenesis and metabolism
  - Showing close correlation between the maximum IRA at DECT and SUVmax on ^{18}F-FDG PET-CT

Schmid-Bindert G, et al. Eur Radiol 2012

Dual-Energy CT (DECT)



- 72 year old patient, SCLC
- A, B : FDG-PET in initial staging
- C : after 2 cycle of therapy, DECT

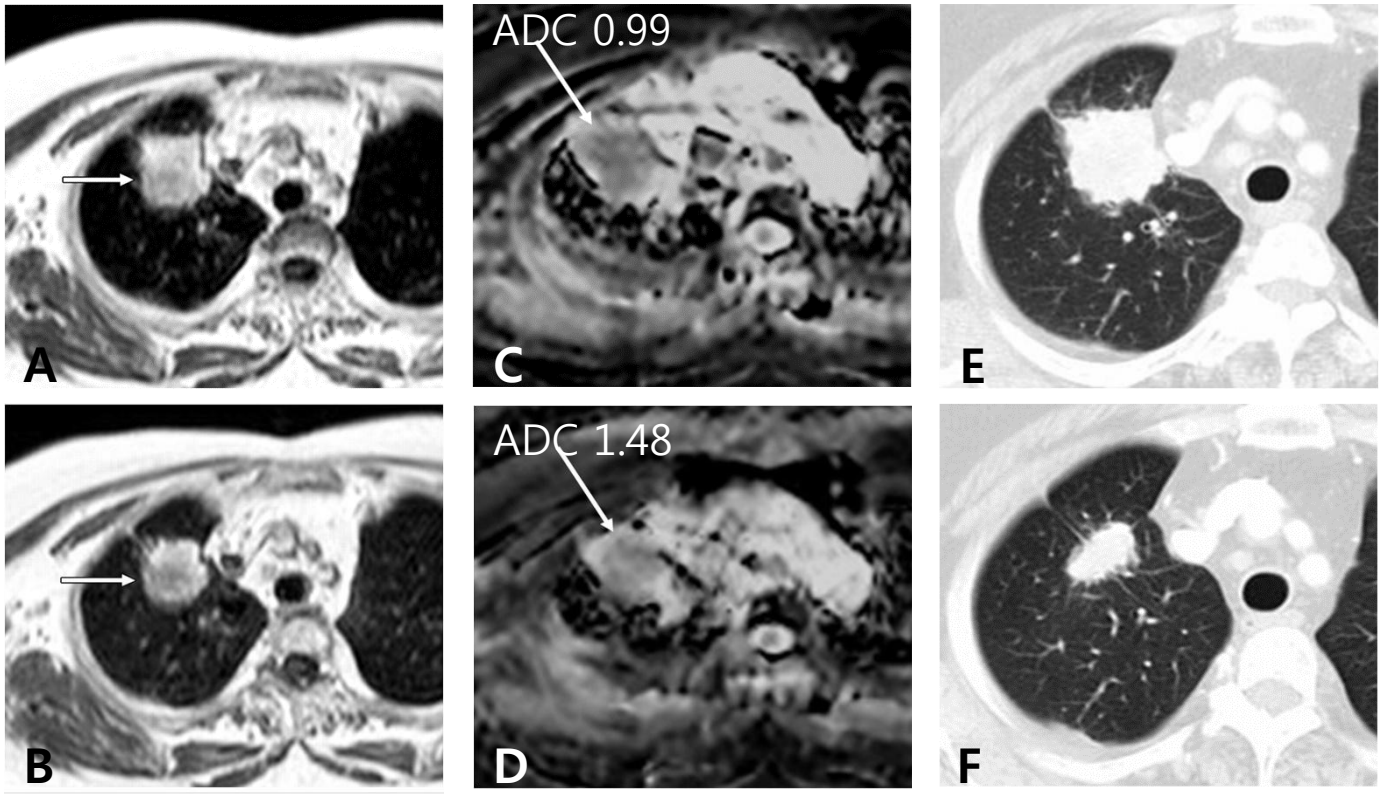
The lower portion of the tumor shows no IRA in the center of the tumor due to central necrosis

Diffusion-Weighted MRI (DWI)

- Analysis of tissue characteristics based on the diffusivity of water molecules
  - Use Apparent Diffusion Coefficient (ADC) mapping
  - DWI provides information about the functional environment of water in tissues, augmenting the morphologic information provided by conventional MRI

Yabuuchi H et al. Radiology 2011

Diffusion-Weighted MRI (DWI)



75 year old patient, Adenocarcinoma, received carboplatin and paclitaxel

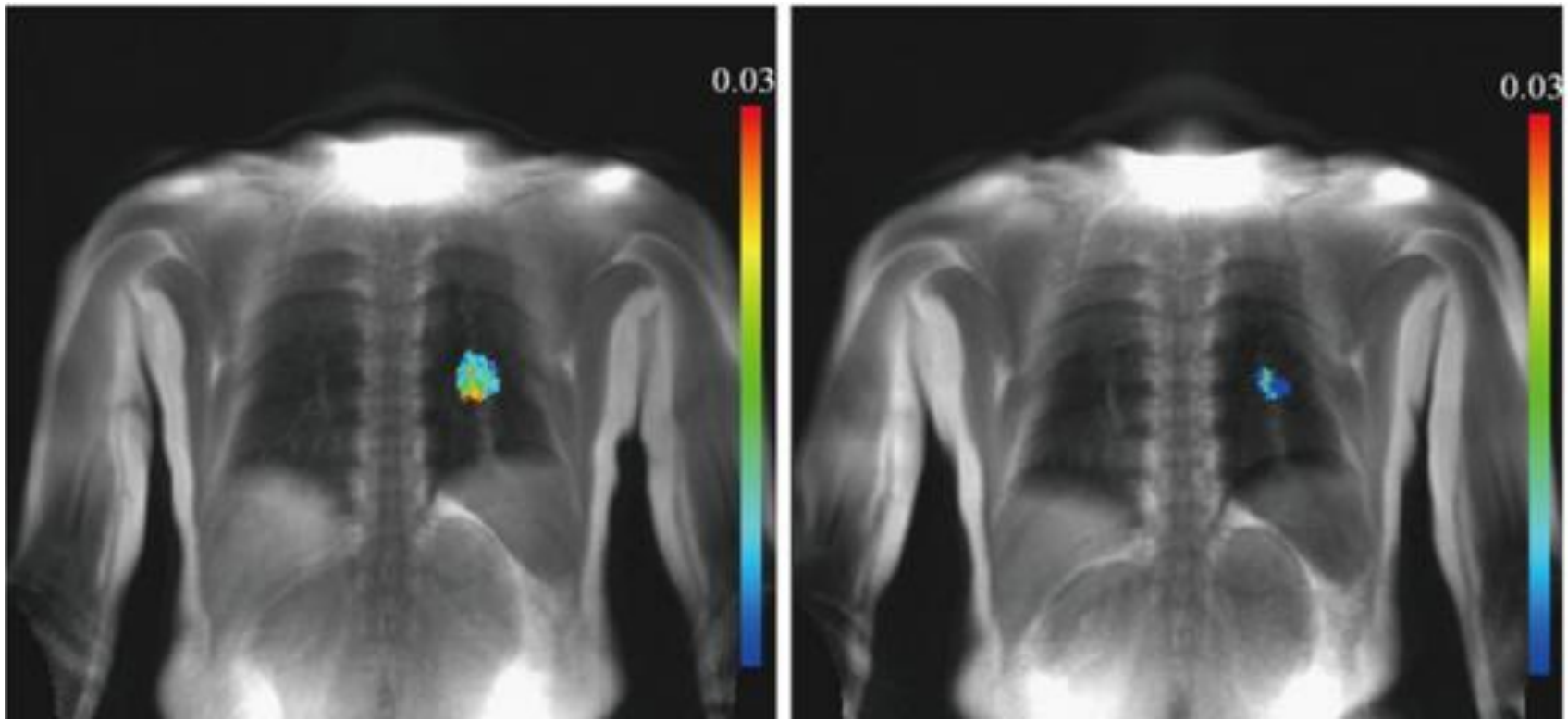
- A, B : T1 weighted MRI, before and after 1 cycle CTx. No size and enhancement change
- C, D : DWI, before and after 1 cycle CTx.
  Indicate that ADC of the lesion (arrow) increased from 0.99 to 1.48
- E, F : Chest CT before and after 2 cycle CTx. Marked decrease of tumor

Dynamic Contrast-enhanced (DCE) MRI

- Dynamic contrast enhancement-magnetic resonance imaging (DCE-MRI) can analysis underlying tumor angiogenesis
  - Utilize parameters relating to tumor perfusion and permeability
  - Analyzed by MR images before and after intravenous injection of contrast agent
- DCE-MRI show successful treatment results in decreases in tumor vascularization and microvessel permeability

Padhani AR et al. Target Oncol 2010

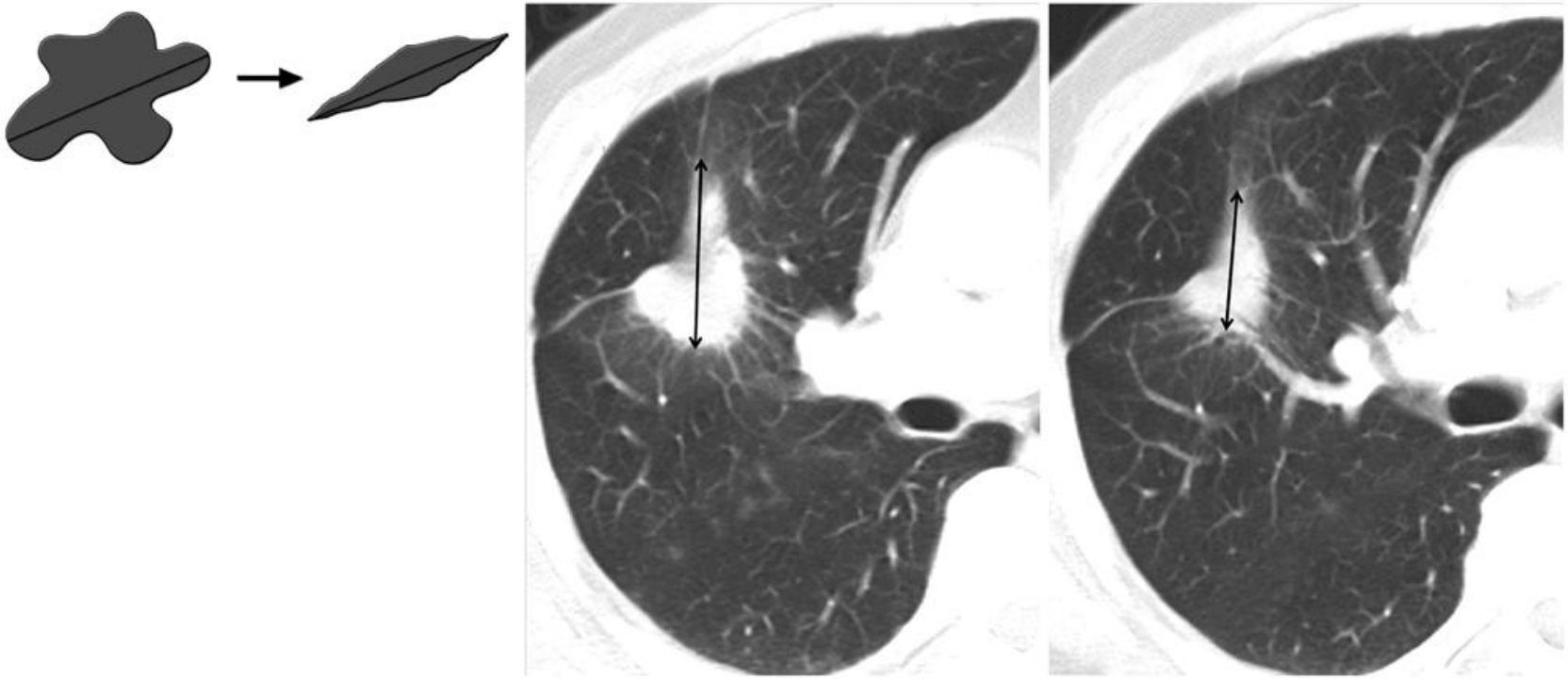
Dynamic Contrast-enhanced (DCE) MRI



- Patient with NSCLC
- After 1st cycle CTx show decrease in size and reduction in perfusion

Padhani AR, Khan AA. Target Oncol 2010

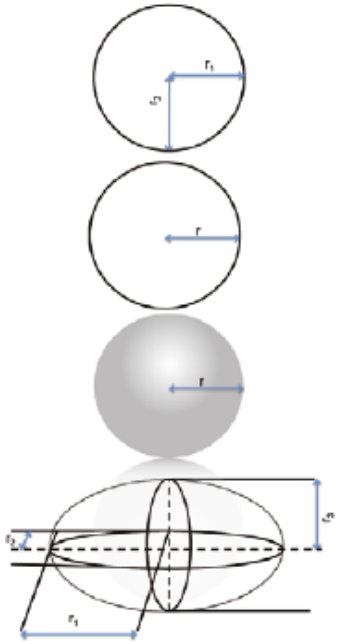
Volumetric Assessment



Limitation of uni-dimensional measurement

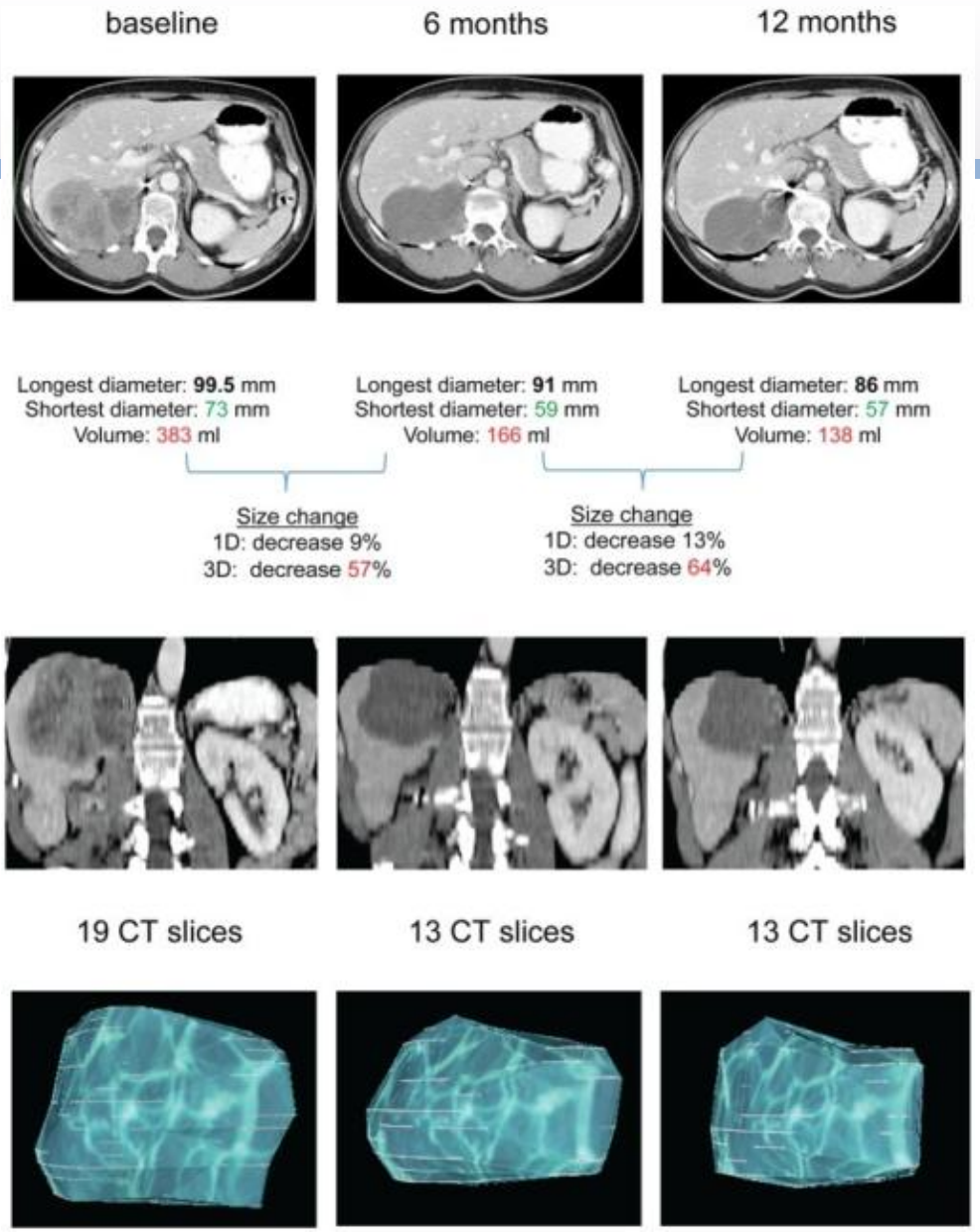
- CT scans on lung window images in patient with NSCLC before
- CTx show decrease of 9.5% (from 4.2 cm to 3.8 cm) in long axis diameter however tumor shrunk by 74% (from 13.6 cm^3 to 3.5 cm^3) in volume

Volumetric Assessment

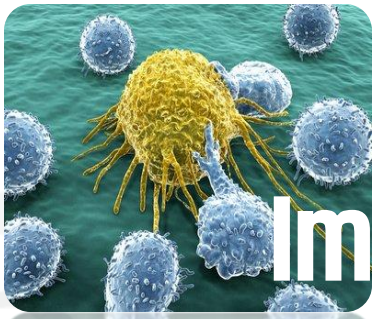


Criteria	Formula	*Partial Response* Decrease	*Progressive Disease* Increase
WHO (2D)	$4\ r_1\ r_2$	50% (S)	25% (S)*
RECIST 1.1 (1D)	$2r$	30% (S)	20% (S)*
Volume Sphere (3D-S)	$4/3\ \pi\ r^3$	65% (S)	73% (S)*
Volume Ellipsoid (3D-E)	$4/3\pi\ r_1\ r_2\ r_3$	30% (S)	20% (S)*
Choi	-	10% (S) or 15% (D, HU)	10% (S)*,**,*** no criteria of PR by D (HU)

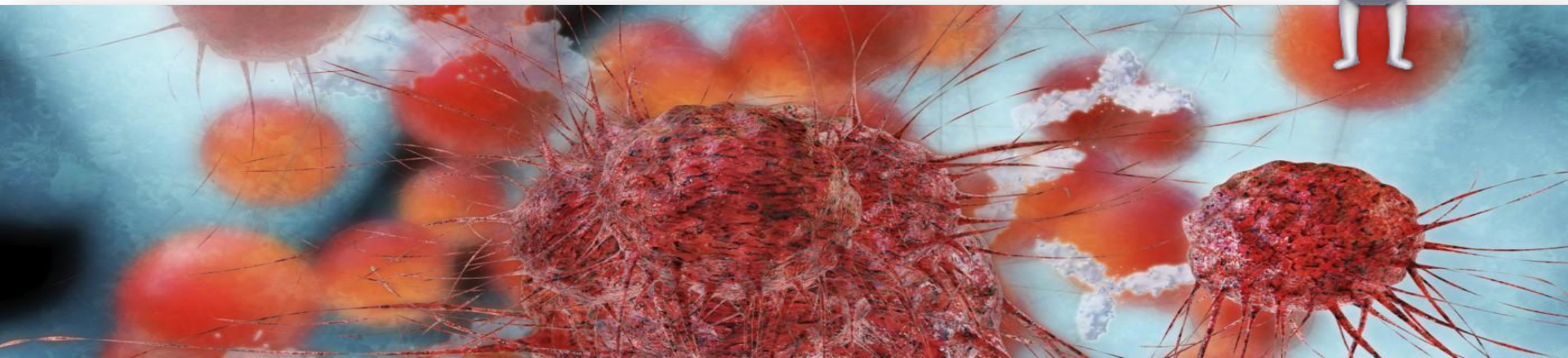
PLoS One. 2012;7(11):e48372



PLoS One. 2012;7(11):e48372



Immunotherapy-related Response Evaluation



Distinct Response Patterns in Immunotherapy

- Two conventional and two that were unique to immunotherapy
  1) Immediate response
  2) Durable stable disease
  3) **Response after tumor burden increase**
  4) **Response in the presence of new lesions**

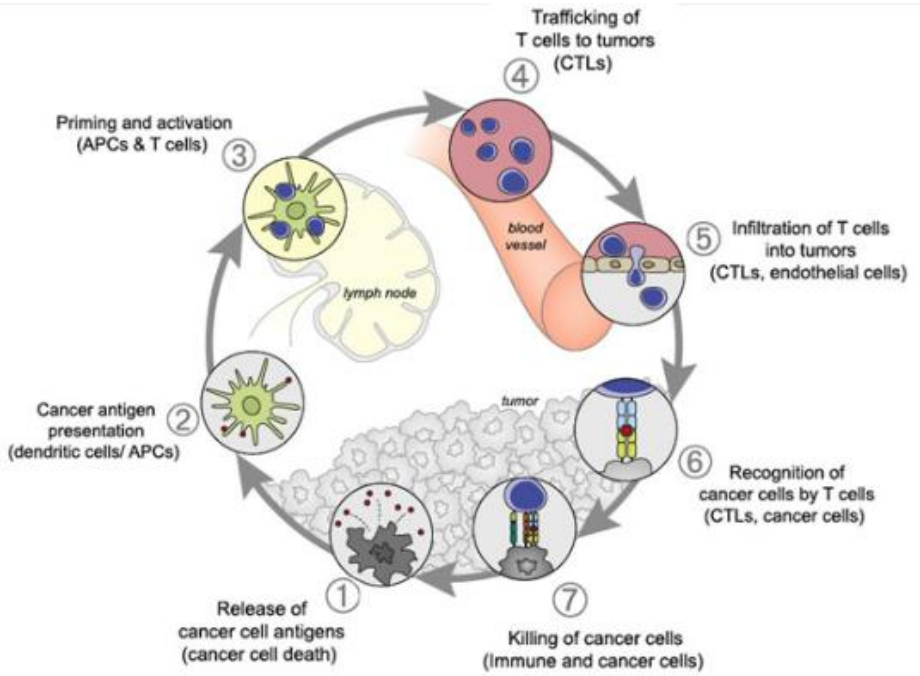
  – These response group based on three large, multinational studies (ipilimumab with melanoma)

Wolchok JD et al. Clin Cancer Res 2009

Weber J et al. Clin Cancer Res 2009

O'Day S et al. Proc Am Soc Clin Onc *2008*

Delayed mechanism of action in immunotherapy



- Reflect dynamics of immune-system
  1) Driving the expansion of T cells
  2) Infiltrate the tumor
  3) Kill tumor cells

- Early increase in tumor burden that is often observed may be a result of the infiltration of T cells into the tumor

Wolchok JD et al. Clin Cancer Res 2009

Weber J et al. Clin Cancer Res 2009

O'Day S et al. Proc Am Soc Clin Onc *2008*

Immune-Related Response Criteria (irRC)

	Conventional WHO criteria	irRC
New measurable lesions	Always represent progressive disease	Incorporated into tumor burden
New non-measurable lesions	Always represent progressive disease	Do not define progression (but preclude irRC)
Measurement of each lesion	Longest diameter (cm)	Longest diameter (cm)
Measurable lesions	≥10 mm in the longest diameter	≥10 mm in the longest diameter
Sum of the measurements	Sum of bidimensional measurements of all target lesions	Sum of unidimensional measurements of all target lesions and any new lesions

Wolchok JD et al. Clin Cancer Res 2009

Nishino M et al. Clin Cancer Res 2013

Immune-Related Response Criteria (irRC)

	Conventional WHO criteria	irRC
Progressive disease (irPD)	Increase in tumor volume ≥25% from nadir, and/or unequivocal progression of non-measurable lesions, and/or appearance of new lesions at any single time point	Increase in tumor volume ≥20% from nadir
Stable disease (irSD)	Not meeting criteria for CR or PR	Not meeting criteria for CR or PR
Partial response (irPR)	Decrease in tumor volume ≥50% relative to baseline	Decrease in tumor volume ≥30% relative to baseline

Wolchok JD et al. Clin Cancer Res 2009

Nishino M et al. Clin Cancer Res 2013

Immune-Related Response Criteria (irRC)

	Conventional WHO criteria	irRC
Complete response (irCR)	Complete disappearance of all lesions	Complete disappearance of all lesion and new measurable lesions
New lesions	Presence of new lesions alone defines progression; new lesions not included in sum of measurements	Presence of new lesions alone does not define progression; measurement of new lesions included in sum of measurements
Confirmation	Confirmation at two consecutive timepoints at least 4 weeks apart	Confirmation at two consecutive timepoints at least 4 weeks apart

Wolchok JD et al. Clin Cancer Res 2009

Nishino M et al. Clin Cancer Res 2013

Limitation of irRC

- Need more prospective trials
- Need more clinical trial other immunotherapies in different cancer types
- Further investigation for the potential association with survival

- irRECIST 2014

ESMO 2014 ABSTRACT 4958

ADAPTATION OF THE IMMUNE-RELATED RESPONSE CRITERIA: irRECIST

Oliver Bohnsack, PAREXEL
Katarina Ludajic, PAREXEL
Axel Hoos, GSK

감사합니다.

김 학 렬 MD, Ph.D.

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보건의료 T2B기반구축사업-호흡기분야

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