RECIST
Response Evaluation Criteria in Solid Tumors

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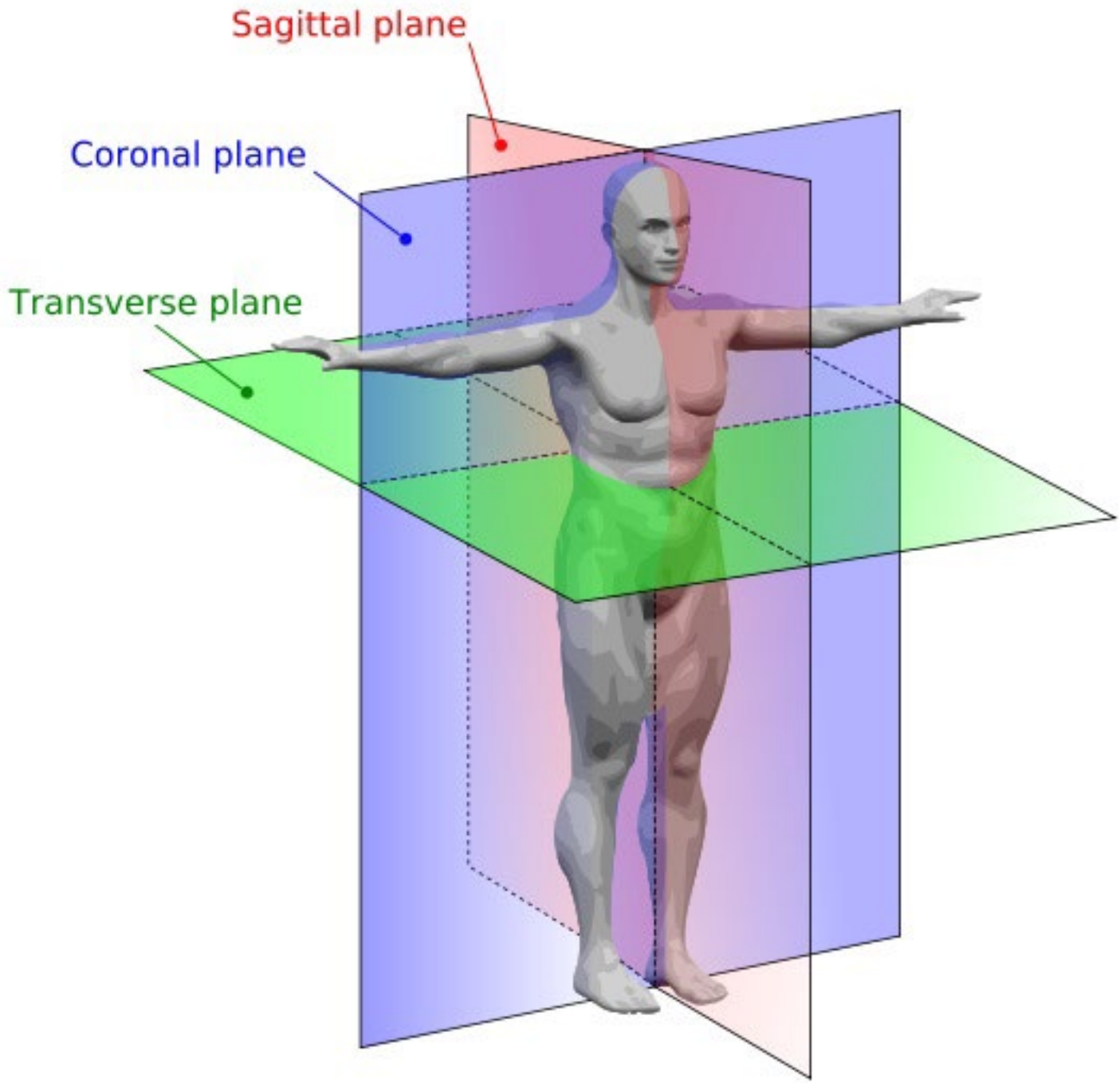
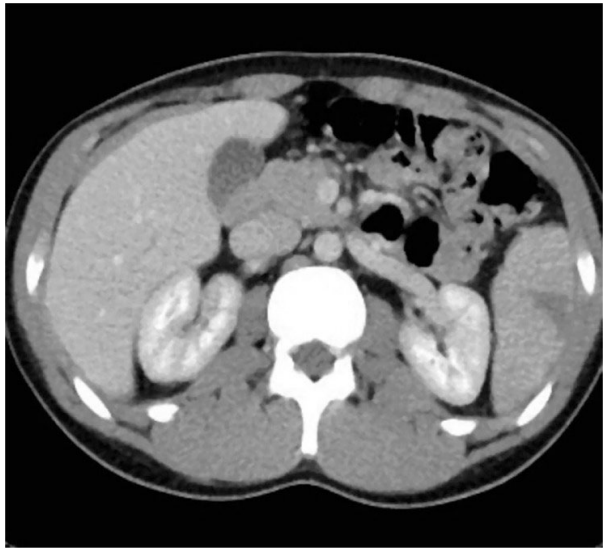
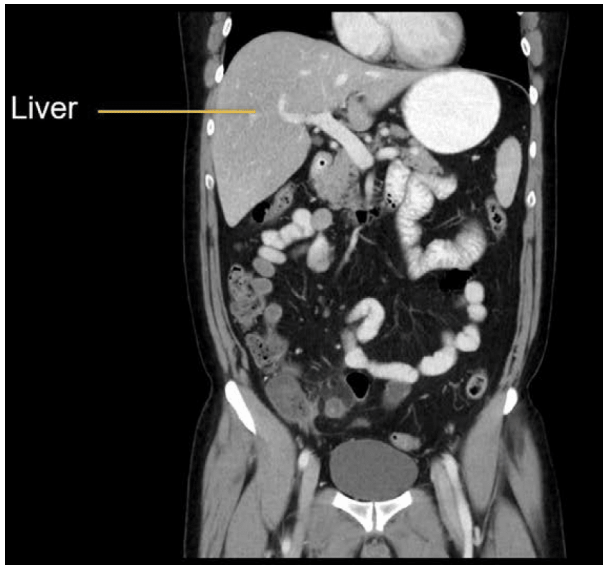
Background

- Tumor regression correlates with overall survival in Ph 3 studies. JCO 2008;10:1346-54.
- 1981: WHO tumor response criteria
  - Sum products of bidimensional lesion
  - Vague language led to 'modification' and confusion in interpretation of results which could alter conclusions
- 2000: RECIST
  - Minimum size of lesion, how many to follow, unidimensional
- 2009: RECIST 1.1
  - Clarified several issues encountered with RECIST

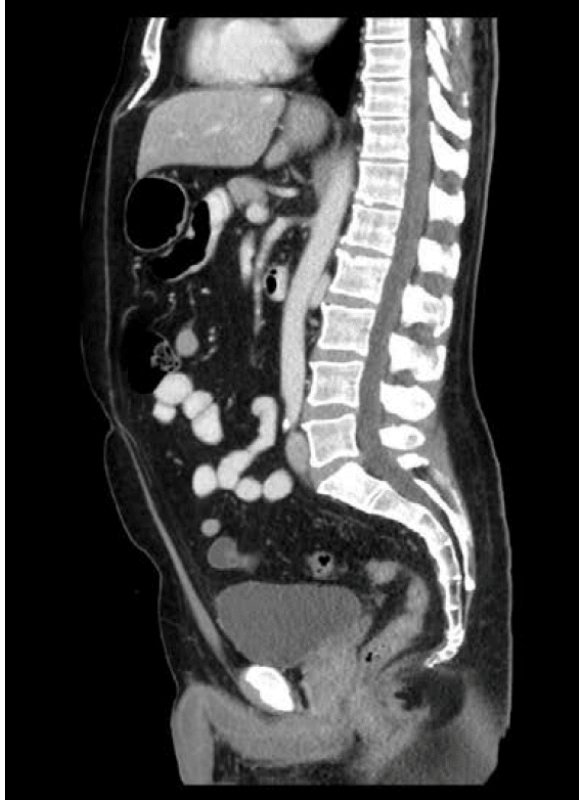

Sagittal plane
Coronal plane
Transverse plane



Transverse Plane



Coronal Plane



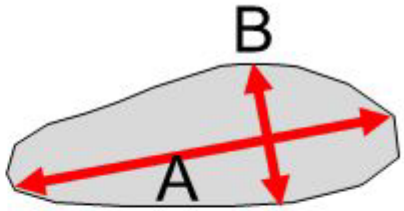
Sagittal Plane

Outline

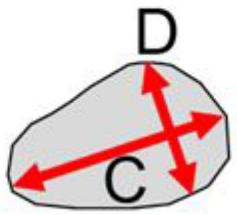
- ”Measurable Disease”
- Baseline Measurements
  - Target Lesions
  - Non-Target Lesions
- Determining response
  - Target Lesions
  - Non-Target Lesions
  - New Lesions
- iRECIST

"Measurable Disease"

- If lesion is not a node: Longest diameter must be ≥ 10 mm
  (A is the longest diameter/B is short axis)
  - Example (A)12 mm x (B) 8 mm
  - Measurable per protocol- YES
  - Example (A) 9 mm x (B) 5mm
  - Measurable per protocol- NO



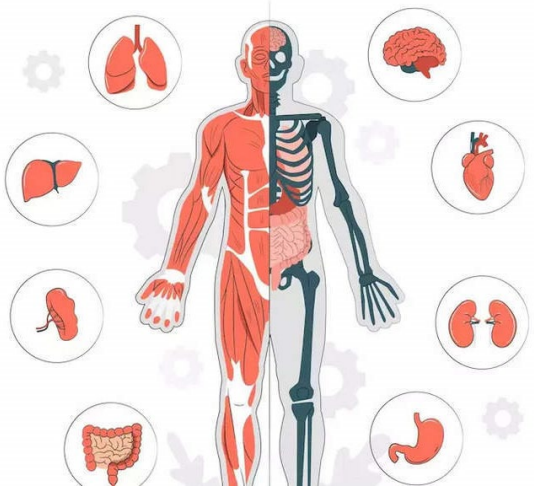
- If lesion is a node: Short Axis must be ≥ 15 mm
  (C is longest diameter/D is short axis)
  - Example (C) 20mm x (D) 16mm
  - Measurable per protocol- YES
  - Example (C) 11 m x (D) 10 mm
  - Measurable per protocol- No



Imaging Modalities Accepted

- CT (With contrast preferred but not mandatory)
- MRI
- Calipers (physical exam) 
- The same mode of measurement should be used throughout the study
  - E.g., If baseline CT without contrast, subsequent CT should be without contrast

Selection of Target Lesions



- Image all areas with known disease
- Maximum of 5 lesions total
- Max 2 lesions per organ/system
- Largest, **most reproducible** lesions
- Lymph nodes
  - Short axis ≥ 15mm
  - If ≥ 10mm but < 15mm should be considered non-target lesion

- Not previously radiated*
- No bone metastases*

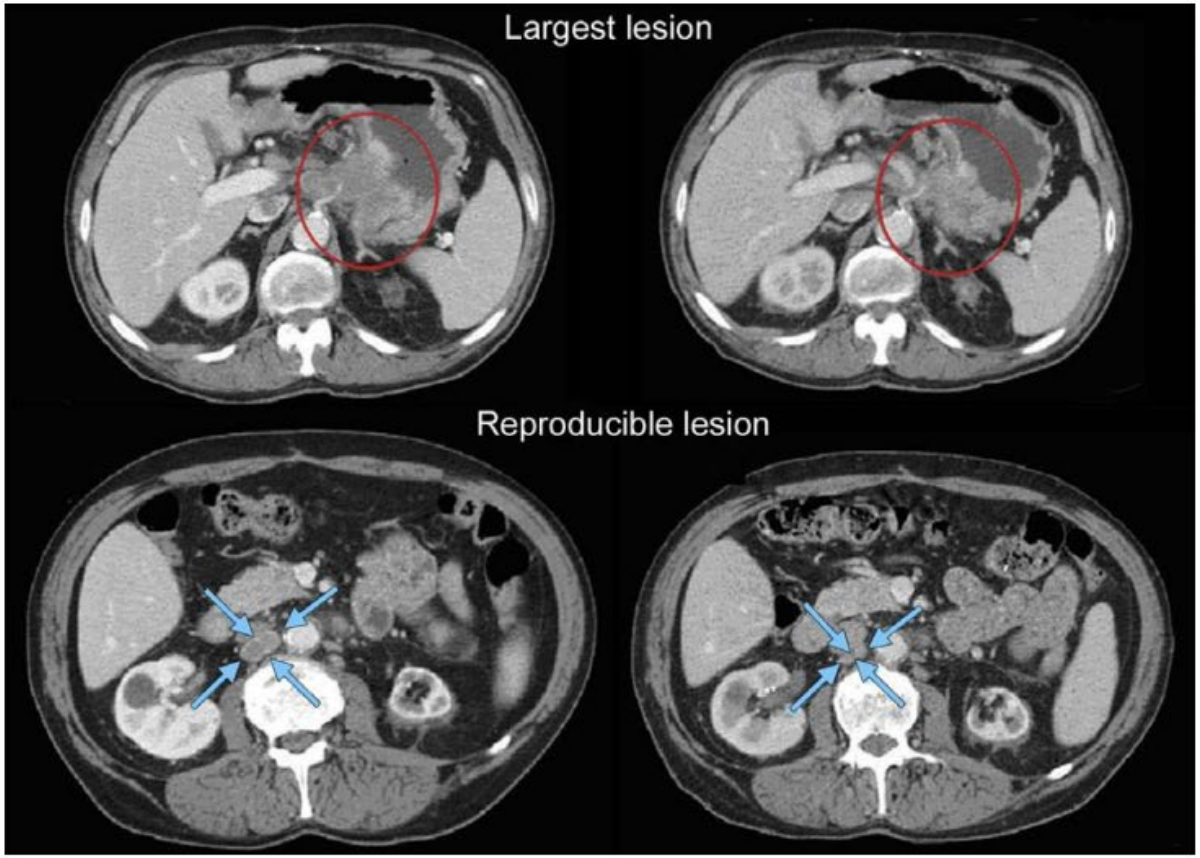


Fig. 3 – Largest lesion may not be most reproducible: most reproducible should be selected as target. In this example, the primary gastric lesion (circled at baseline and at follow-up in the top two images) may be able to be measured with thin section volumetric CT with the same degree of gastric distention at baseline and follow-up. However, this is potentially challenging to reproduce in a multicentre trial and if attempted should be done with careful imaging input and analysis. The most reproducible lesion is a lymph node (circled at baseline and at follow-up in the bottom two images).

Non-Target Lesions (Baseline)

- Lymph nodes as above
- Measurements **NOT RECORDED**
- Can record multiple non-target lesions involving the same organ as a single item on case record form
  - "Multiple enlarged pelvic lymph nodes" or "Multiple liver metastases"
- Previously radiated lesions*

Common Pitfalls

- Target lesions assigned at BASELINE only
- Non-target lesions NEVER get measured, even if they become "measurable" (e.g., lymph node growing to > 15mm)
- Ensure target lesions were not previously radiated

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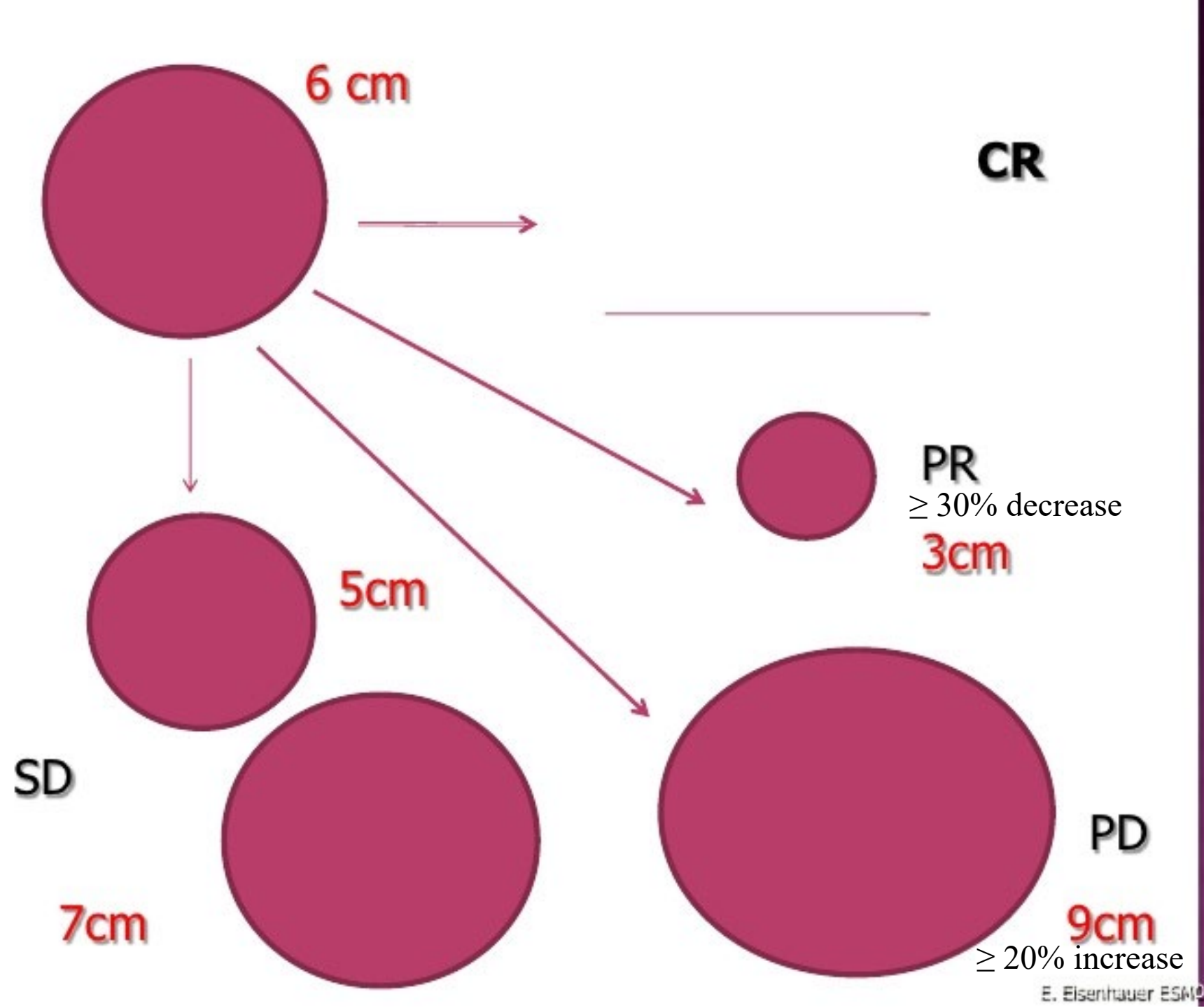

6 cm
CR
PR
≥ 30% decrease
3cm
5cm
SD
7cm
PD
9cm
≥ 20% increase
E. Eisenhauer ESMO ECLU Jul 2007

Response Criteria

4.3. *Response criteria*

This section provides the definitions of the criteria used to determine objective tumour response for target lesions.

4.3.1. *Evaluation of target lesions*

Complete Response (CR): Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.

Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

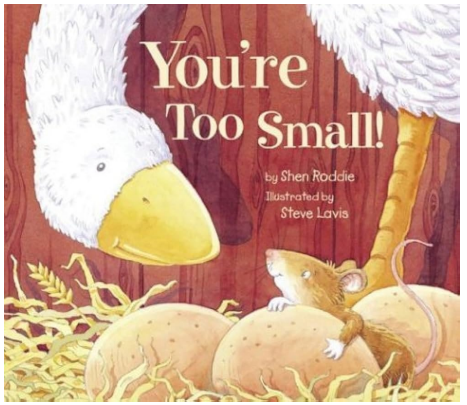
Progressive Disease (PD): At least a 20% increase in the sum of diameters of target lesions, taking as reference the *smallest sum on study* (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. (*Note*: the appearance of one or more new lesions is also considered progression).

Stable Disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study.

Assessment of Lymph Nodes

- If < 10mm this qualifies as CR
- Record measurement even if shrinks to < 10mm
- Measurement important to not overstate progression if nodes increase

‘too small to measure’



- Record actual measurements of target lesions even if very small (e.g. 2mm)
- If radiologist feels the lesion has disappeared, measurement should be recorded as 0
  - Radiologist may mark as ‘-’ or 0

- If lesion is present but cannot measure, default value of 5mm assigned
  - Radiologist will mark as ‘+’

Non-target lesions

- ‘Unequivocal Progression’

  - Overall level of substantial worsening in non-target disease
  - A modest ‘increase’ in the size of one or more lesions usually not sufficient
  - Often requires discussion between radiologist and clinician. May take into account clinical status of patient (increase in pain etc)

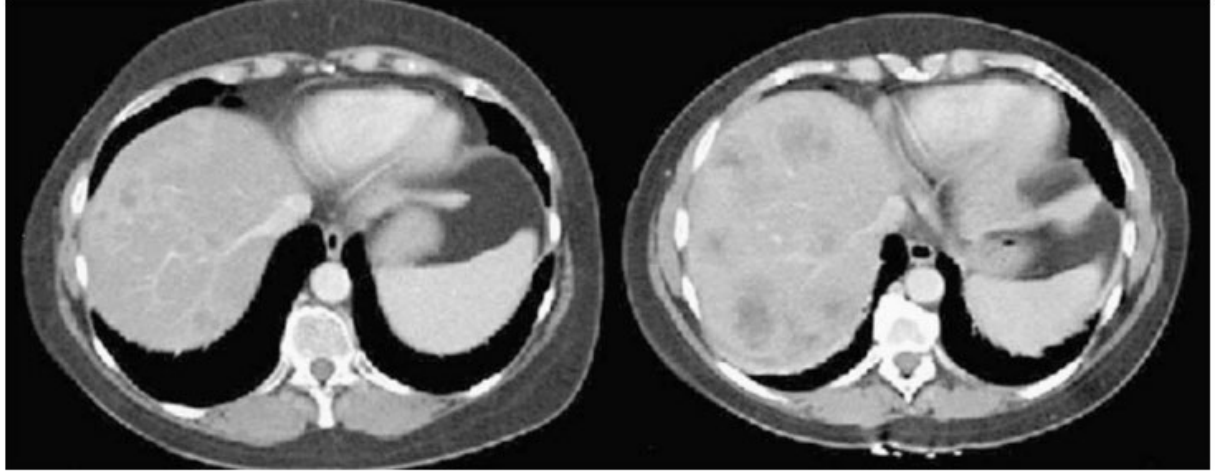


Fig. 5 – Example of unequivocal progression in non-target lesions in liver.

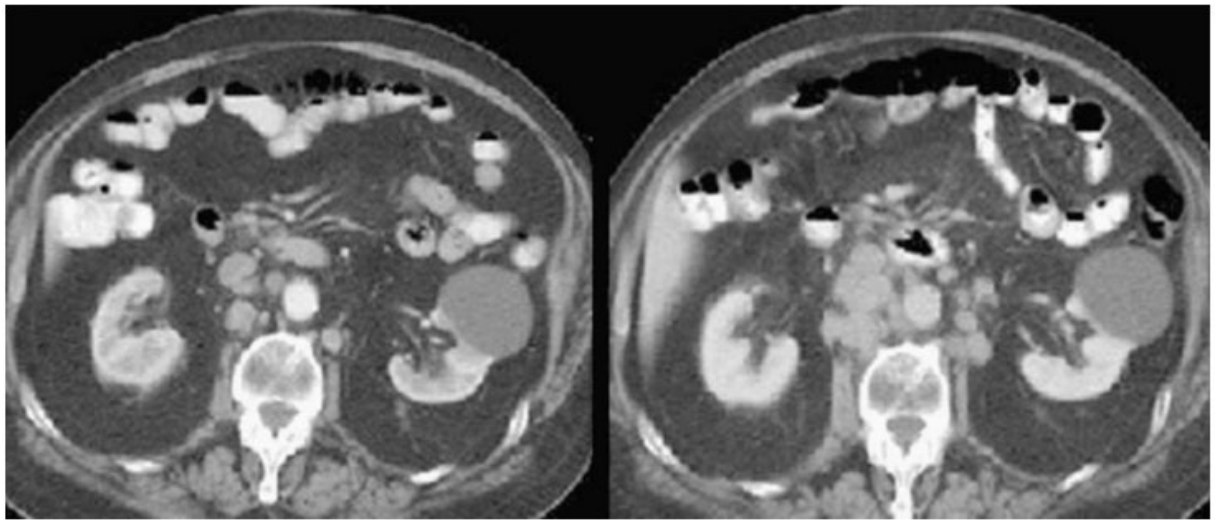


Fig. 6 – Example of unequivocal progression in non-target lesion (nodes).

Non-target lesions

Complete Response (CR): Disappearance of all non-target lesions and normalisation of tumour marker level. All lymph nodes must be non-pathological in size (<10 mm short axis).

Non-CR/Non-PD: Persistence of one or more non-target lesion(s) and/or maintenance of tumour marker level above the normal limits.

Progressive Disease (PD): *Unequivocal progression* (see comments below) of existing non-target lesions. (*Note:* the appearance of one or more new lesions is also considered progression).

New Lesions

- Should not be due to differences in:
  - Scanning technique
  - Different imaging modality (CT vs MRI vs PET)
- Lesion identified on follow-up in a location NOT scanned at baseline WILL be considered new and is disease progression
  - E.g. brain mets discovered on study
- No specific criteria for definition of new lesion (no size cutoff) but must be **unequivocal**

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Timeline of radiographic criteria

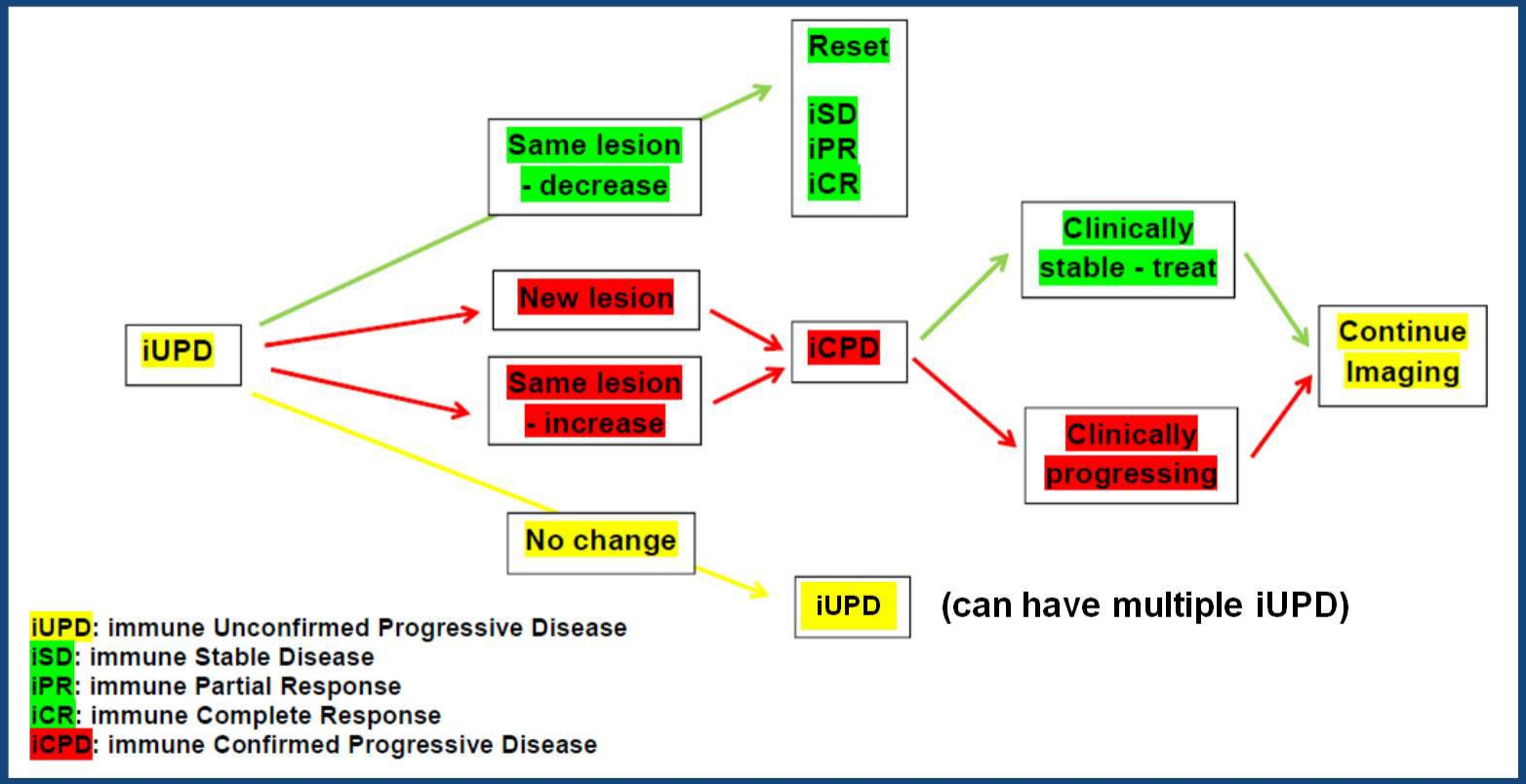
Year	Criteria	Journal
1981	WHO	Cancer
2000	RECIST	Eur J Cancer
2009	RECIST 1.1	JNCI
2009	irRC	Clin Cancer Res
2013	irRECIST	Clin Cancer Res
2017	iRECIST	Lancet Oncology
2018	imRECIST	J Clin Oncol

Comparing RECIST to iRECIST

	RECIST 1.1	iRECIST
Measurement modality	Unidimensional	Unidimensional
Baseline lesion size	≥ 10mm	≥ 10mm
Baseline lesion number	5 lesions in total; 2 per organ	5 lesions in total; 2 per organ
Appearance of new lesions	PD	iUPD; not incorporated into sum; may turn into iCPD
CR	Disappearance of all lesions	Disappearance of all lesions
PR	≥ 30% decrease from baseline	≥ 30% decrease from baseline
SD	Neither CR nor PD is met	Neither CR nor PD is met
PD	≥ 20% increase; minimum of 5mm	≥ 20% increase; minimum of 5mm
Confirmation of PD	Not applicable	Yes; 4-8 weeks

Presented By Sanjay Goel at 2018 ASCO Annual Meeting

iUPD: The key new phenomenon in iRECIST



Presented By Sanjay Goel at 2018 ASCO Annual Meeting

Key features of iRECIST

- If iUPD, and clinically stable, continue therapy
- Clinically stable includes
  - Stable performance status
  - No increase in disease related symptoms
  - No increase in need for managing symptoms
- New lesions are not added to sum of baseline
- Once iCPD, initial date of iUPD is date of PD

↑ iUPD ↑ iSD ↑ iUPD ↑ iCPD

Seymour, Lancet Oncology, 2017

Case #1

Circle "Yes" for target lesions and "No" for non-target lesions in Target Lesion column.

Tumor #	Disease Description/location	Target Lesion	Method of Meas.	Date 6/9/20 BL	Date 9/8/2020	Date 11/3/20	Date 12-28-20	Date
1	LUL lung nodule	(Yes)/No	CT	1.3cm (79)	0	0	0	
2	Other lung nodules	Yes/(No)	CT	+	+	+	+	
3	Pericardial nodule	(Yes)/No	CT	2.1cm (101)	2.4cm (100)	2.6cm (109)	3.0cm (100)	
4	(L) paratracheal mass	(Yes)/No	CT	4.8cm (36)	3.2cm (33)	2.8cm (31)	3.5cm (23)	
5	T3 vert. body lesion	Yes/(No)	CT	+ (40)	+ (38)	+	+	
6		Yes/No						
7		Yes/No						
8		Yes/No						
9		Yes/No						
10		Yes/No			(back)		(back)	
	Signature of physician evaluating response			[redacted]				
	Sum total			8.2 6.9cm	5.6cm	5.4		
	Record % change at each evaluation			[redacted]	-31.7%		-20.7%	
Overall response: Indicate for each column overall response.					PR		Stable	

Case #2

Tumor #	Disease Description/location	Target Lesion	Method of Meas.	Date 3/5/19	Date 4/15/19	Date 5/20/19	Date 7/19/19	Date 9/1/19
1	Rt lower paratracheal node	(Yes)/No	CT	(2-31) 2.0cm	(2-29) 1.8cm	(2-41) 1.1cm	(36) 1.0cm	(33) 1.0cm
2	Subcarinal node	(Yes)/No	CT	(2-42) 1.5 cm	(2-40) 1.5cm	(2-57) 1.7cm	(44) 1.6cm	(40) 1.9cm
3	RUL mass	(Yes)/No	CT	(2-27) 5.1cm	(2-26) 4.0cm	(2-33) 3.6cm	(26) 3.4cm	(24) 3.8cm
4		Yes/No						
5		Yes/No						
6		Yes/No						
7		Yes/No						
8		Yes/No						
9		Yes/No						
10		Yes/No						
	Signature of physician evaluating response			[redacted]				
	Sum total			8.6	7.3	6.4	6.0	6.7
	Record % change at each evaluation			Baseline	↓15%	↓26%	↓30%	↓21%
Overall response: Indicate for each column overall response.					SD	SD	PR	SD

11.7% increase (PR)

Case #2

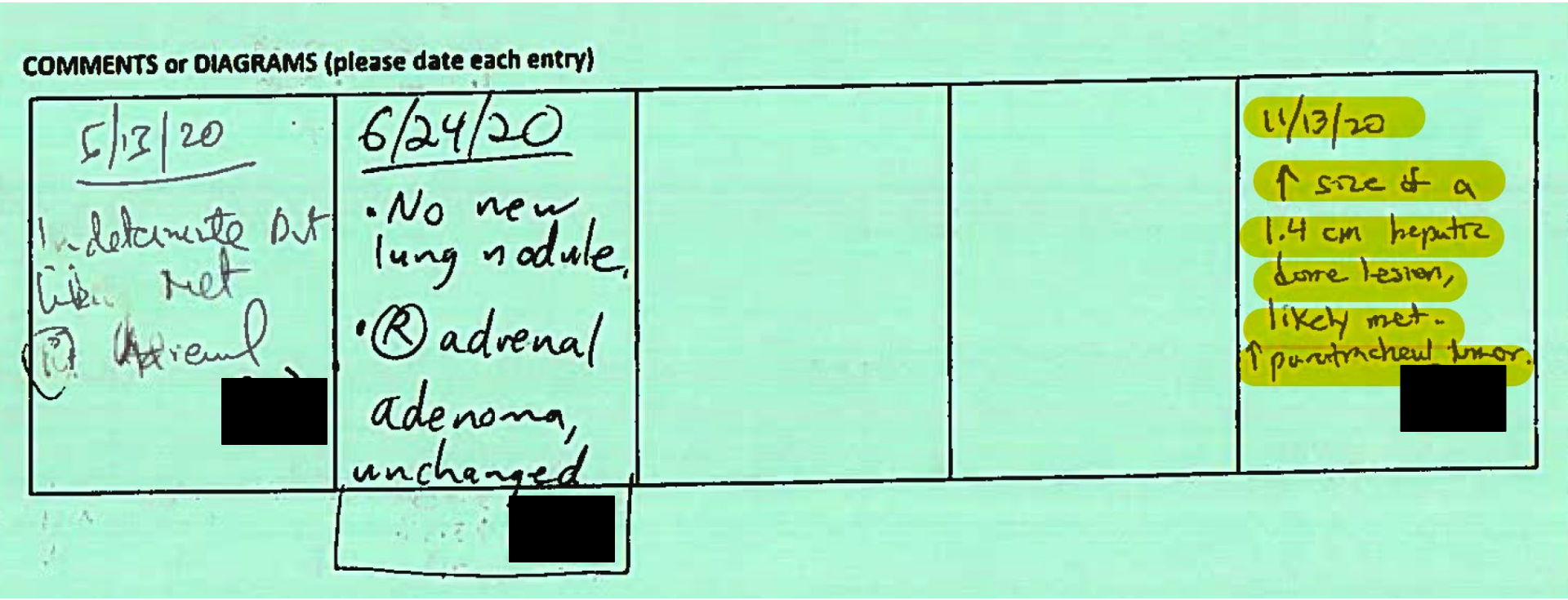
Tumor #	Disease Description/location	Target Lesion	Method of Meas.	Date 10/22/19	Date	Date	Date	Date
1	Rt lower paratracheal node	(Yes)/No	CT	(45) 1.3 cm				
2	Subcarinal node	(Yes)/No	|	(53) 2.1 cm				
3	RUL mass	(Yes)/No	|	(37) 4.1 cm				
4		Yes/No						
5		Yes/No						
6		Yes/No						
7		Yes/No						
8		Yes/No						
9		Yes/No						
10		Yes/No						
	Signature of physician evaluating response			[redacted]				
	Sum total			7.5				
	Record % change at each evaluation			↓13% SD				
Overall response: Indicate for each column overall response.								

25% increase (PD)

Case #3

Tumor #	Disease Description/location	Target Lesion	Method of Meas.	Date BL 5/13/20	Date 6/24/20	Date 8/5/20	Date 9/25/20	Date 11/13/20
1	(RT) lower lobe lung nodule	Yes/No	CT	1.8 cm [114]	2.0 cm [105]	1.8 cm [118]	1.7 cm [106]	(101) 2.2cm
2	(LT) lower lobe lung	Yes/No	CT	1.8 cm [88]	1.9 cm [76]	2.1 cm [87]	2.1 cm [87]	(94) 2.2cm
3	Other lung Nodules	Yes/No	CT	+	+	+	+	+
4	Subcarinal Node	Yes/No	CT	1.5 cm [66]	1.4 cm [60]	1.2 cm [68]	1.4 cm [63]	(66) 1.6cm
5	Retrobulbar brain	Yes/No	CT	+	+	+	+	+
6		Yes/No						
7		Yes/No						see back
8		Yes/No						
9		Yes/No						
10		Yes/No						
	Signature of physician evaluating response							
	Sum total			5.1 cm	5.3 cm	5.1 cm	5.2 cm	5.1 cm
	Record % change at each evaluation				↑ 3.9%	0%	↑ 1.9%	↑ 17.6%
Overall response: Indicate for each column overall response.				BL	SD	SD	SD	SD

Case #3


COMMENTS or DIAGRAMS (please date each entry)
5/13/20
Indeterminate RLL
[redacted]
6/24/20
• No new lung nodule.
• ® adrenal adenoma, unchanged
[redacted]
11/13/20
↑ size of a 1.4 cm hepatic dome lesion, likely met.
↑ paratracheal tumor.
[redacted]