4th INTERNATIONAL WORKSHOP ON INTERIM-PET IN LYMPHOMA

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international workshop for PET in lymphoma staging and restaging

Lale Kostakoglu
Department of Radiology
Mount Sinai Medical Center, New York, USA

Imaging Task Force Recommendations for Staging

- FDG PET-CT should be used for staging in routine clinical practice and in clinical trials *(category 1)*
- FDG PET-CT can be used to
  - image/stage most subtypes of lymphoma and
  - target biopsy
- FDG PET-CT is not routinely recommended in lymphomas with low FDG avidity e.g. CLL/SLL, extranodal MZL and some cutaneous lymphomas *(category 1)*
- PET-CT with ceCT is desirable for staging patients likely to undergo radiotherapy ideally within a single scanning session
  - a two stage approach with unenhanced PET-CT followed by regional ceCT for equivocal lesions may be preferred taking into account age, disease type, stage *(category 2)*

disease-based → individualized

prognostic indices increasingly favored over staging alone but staging is an integral part of the established prognostic scoring systems in lymphoma (IPI, IPS)

Staging remains fundamental to risk-stratify pts and select the appropriate treatment strategy

- **Ann Arbor staging (1971), most widely used system, evolved to incorporate CT (Cotswolds, 1989) into clinical algorithm although CT has significant flaws**

- **Contrary to HL, NHL pts present with advanced stage and END, AA system is only powerful when used with other prognostic factors (IPI)** Shipp M, N Engl J Med 1993;329:987

- **FDG-PET proved to be a more accurate staging tool than CT; max joint sensitivity and specificity of 88%**

Radford, J Clin Oncol 1988;6, Lister, J Clin Oncol, 1989:7:1630, Rosenberg. Cancer Treat Rep, 1977;61:1023, Nyman, Acta Radiol, 1996:37, Menzel, Acta Oncol 2002;41, Naumann, Br J Cancer 2004;90, Partridge, Ann Oncol 2000;11, Freudenberg, EJNM 2004;31., Isasi, Cancer, 2005;104, Hutchings, Haematologica, 2006;91, Schaefer, Radiology 2004;232, Naumann, Br J Cancer,2004;90, Tatsumi, Radiology, 2005; 237:

.

- Discordance btwn PET and CT findings occurs in up to 30% of pts at staging, in favor of PET/CT imaging
- FDG PET leads to upstaging in 20-30% of pts, but stage migration from early to advanced stage disease is rare

Study	No. of Patients With HL	No. of Patients With NHL	Upstage (%)	Downstage (%)	Change in Therapy (%)
Bangerter[20]	44		12	2	14
Partridge[23]	44		40.9	< 10	25
Buchman[16]	27	25	8	0	8
Jerusalem[21]	33		1	1	1
Weihrauch[24]	22		18	0	5
Wirth[25]	19	31	14	0	18
Munker[26]	73		29	3	< 1
Raanani[27]			32	15	45
Hutchings[18]	99		17	5	7
Rigacci[22]	186		14	1	7
Pelosi[19]	30		10		7
Pelosi[19]		35	11.4		9

Bruce C, J Clin Oncol, 2011;29:1844

Naumann, Br J Cancer 2004;90, Isasi, Cancer, 2005;104, Hutchings, Haematologica, 2006;91, Weihrauch, Ann Hematol, 2002;81, Jerusalem, Haematologica 2001;86 Picardi, Ann Oncol.2011; 22

FDG PET/CT Staging in Lymphoma

- Likelihood of a change in treatment ~15%, with no data supporting improvement in pt outcome
  - widespread use of systemic chemo mitigates the need for exact definition of disease extent
  - conversely, recent trend for individualized rx; de-escalation and limit RT to involved LNs requires more precise info on the anatomic extent of disease

- PET/CT as the most sensitive staging modality is of particular value for those pts with apparently early stage disease

- Staging PET/CT essential for evaluation of subsequent therapy response

Hutchings M, Haematologica 2006;91:482, Pelosi E, Radiol Med 2008;113:578, Jerusalem G, Haematologica 2001;86:266, Rigacci L, Ann Hematol 2007;86:897, Weihrauch MR, Ann Hematol 2002;81:20, Wirth A, Am J Med 2002;112:262, Munker R, Ann Oncol 2004;15: 1699, Raanani P, Ann Oncol 2006;17, Kabickova E, EJNMMI 2006;33, Schaefer NG, Radiology. 2004; 232, Tatsumi M Radiology 2005; 237, Partridge S. Ann Oncol 2000;11

It is recommended that PET-CT be used for staging in routine clinical practice and in clinical trials (*category 1*)

FDG avidity among lymphomas

- DLBCL, HL and FL are invariably FDG avid
- Less common aggressive lymphomas; Burkitts, NK-T cell, lymphoblastic, MCL, anaplastic large T-cell are FDG avid
- Variable and/or low grade FDG avidity,
  - CLL/SLL, extranodal marginal zone lymphoma (MZL)
  - angioimmunoblastic T-cell (AITL), cutaneous lymphomas (PTCL)

Tsukamoto, Cancer 2007;110, Le Dortz, JNMMI, 2010;37:, Wöhrer, Ann Oncol 2006;17, Perry, Eur J Haematol 2007;79, Kako, Ann Oncol, 2007;18:, Elstrom, Blood, 2003;101, Brepoels, Leuk Lymphoma 2008;49

Histology	Weiler-Sagie (*n* = 766)	Tsukamoto (*6*) (*n* = 255)	Elstrom (*5*) (*n* = 172)	Other publications
Hodgkin disease	100% (*n* = 233)	97% (*n* = 23)	98% (*n* = 47)	Rigacci (*24*) 100% (*n* = 186)
Burkitt lymphoma	100% (*n* = 18)	100% (*n* = 5)	100% (*n* = 1)	
Mantle cell lymphoma	100% (*n* = 14)	100% (*n* = 9)	100% (*n* = 7)	Gill (*25*) 100% (*n* = 9)
Anaplastic large T-cell lymphoma	100% (*n* = 14)	100% (*n* = 5)	100% (*n* = 2)	
Marginal zone lymphoma, nodal	100% (*n* = 8)			Hoffmann (*18*) 83% (*n* = 6)
Lymphoblastic lymphoma	100% (*n* = 6)			
Angioimmunoblastic T-cell lymphoma	100% (*n* = 4)	100% (*n* = 5)		Kako (*8*) 100% (*n* = 4)
Natural killer/T-cell lymphoma	100% (*n* = 2)	100% (*n* = 7)	100% (*n* = 1)	Karantanis (*26*) 100% (*n* = 10), Kako (*8*) 100% (*n* = 8)
Diffuse large B-cell lymphoma	97% (*n* = 222)	97% (*n* = 81)	100% (*n* = 51)	Lin (*27*) 100% (*n* = 92)
Follicular lymphoma	95% (*n* = 140)	91% (*n* = 44)	98% (*n* = 42)	Karam (*9*) 100% (*n* = 17)
Peripheral T-cell lymphoma	90% (*n* = 10)	98% (*n* = 9)	40% (*n* = 5)	Bishu (*20*) 86% (*n* = 24), Kako (*8*) 91% (*n* = 11)
Small lymphocytic lymphoma	83% (*n* = 29)	50% (*n* = 4)	100% (*n* = 1)	Karam (*9*) 47% (*n* = 15)
Enteropathy-type T-cell lymphoma	67% (*n* = 3)			Hoffmann (*23*) 100% (*n* = 4), Hadithi (*22*) 100% (*n* = 8)
Marginal zone lymphoma, unspecified			67% (*n* = 12)	
Marginal zone lymphoma, splenic	67% (*n* = 3)	53% (*n* = 10)		
MALT marginal zone lymphoma	54% (*n* = 50)	82% (*n* = 52)		Perry (*10*) 55% (*n* = 33), Radan (*19*) 71% (*n* = 24), Alinari (*16*) 81% (*n* = 26), Beal (*17*) 81% (*n* = 42)
Lymphomatoid papulosis	50% (*n* = 2)			
Primary cutaneous anaplastic large T-cell lymphoma	40% (*n* = 5)			Kako (*8*) 60% (*n* = 5)
Mycosis fungoides			100% (*n* = 1)	
Subcutaneous paniculitis-like T-cell lymphoma		71% (*n* = 1)		
Cutaneous B-cell lymphoma			0% (*n* = 2)	

Weiler-Sagie M, J Nucl Med 2010;51:25

- PET/CT should be the imaging modality of choice for FDG-avid lymphomas including HL, DLBCL, Burkitt, and other aggressive NHLs, FL

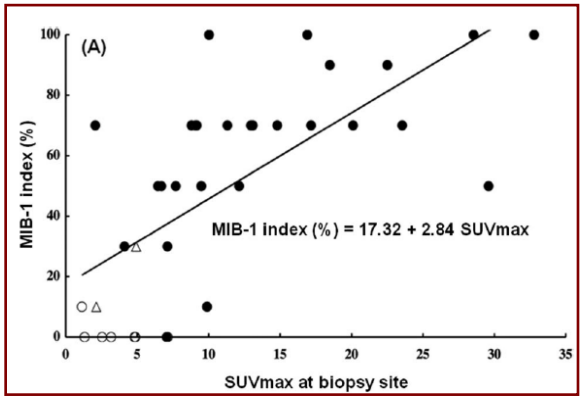
- For those lymphoma subtypes including CLL/SLL, MZL and MCL staging with FDG PET should be decided in the context of clinical necessity

Intensity of FDG uptake is higher in aggressive than indolent lymphomas: transformation

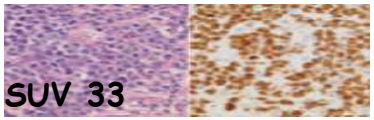
- SUVs exceeding 10 yields a 81% specificity for the identification of an aggressive behavior

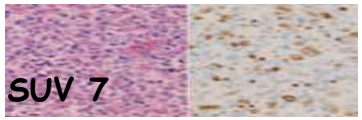
  Schoder H, J Clin Oncol 2005; 23:4643, Noy A, Ann Oncol. 2009;20:508

- Positive correlation observed btw SUVmax at the bx site and Ki-67 proliferation index (MIB-1) in NHL (r =0.69, p < 0.001)



Watanabe R, Leuk Lymph 2010;51:279





- Clinical suspicion for transformation should prompt a FDG PET/CT to guide biopsies to sites with highest FDG avidity to dx transformation and timely institute proper treatment

FDG PET/CT can be used to image most subtypes of lymphomas and to target biopsy (*category 1*).

Role of Contrast-Enhanced CT

- Whether or not to perform PET/ceCT vs PET/ldCT is controversial
- Better sensitivity and specificity reported for FDG PET vs ceCT in detection of nodal and extranodal HL
- Addition of ceCT to PET/ldCT shown no significant difference in lesion detection rate, except for occasional upstaging
- Additional ceCT changed management in <10% of pts while PET/ldCT resulted in a change in almost 50% of HL pts compared with CECT alone

Hutchings, Haematologica 2006;91 , Schaefer, Radiology. 2004;232, Tatsumi Radiology 2005; 237, Partridge. Ann Oncol 2000;11,, Raanani, Ann Oncol 2006;17, Elstrom, Ann Oncol 2008;19, Rodríguez-Vigil, J Nucl Med 2006;47, Pinilla, Q J Nucl Med Mol Imaging 2011;55

Role of Contrast-Enhanced CT

Cumulative data suggest a marginal benefit with the addition of ceCT to PET/CT but ceCT can resolve indeterminate findings and lead to occasional upstaging

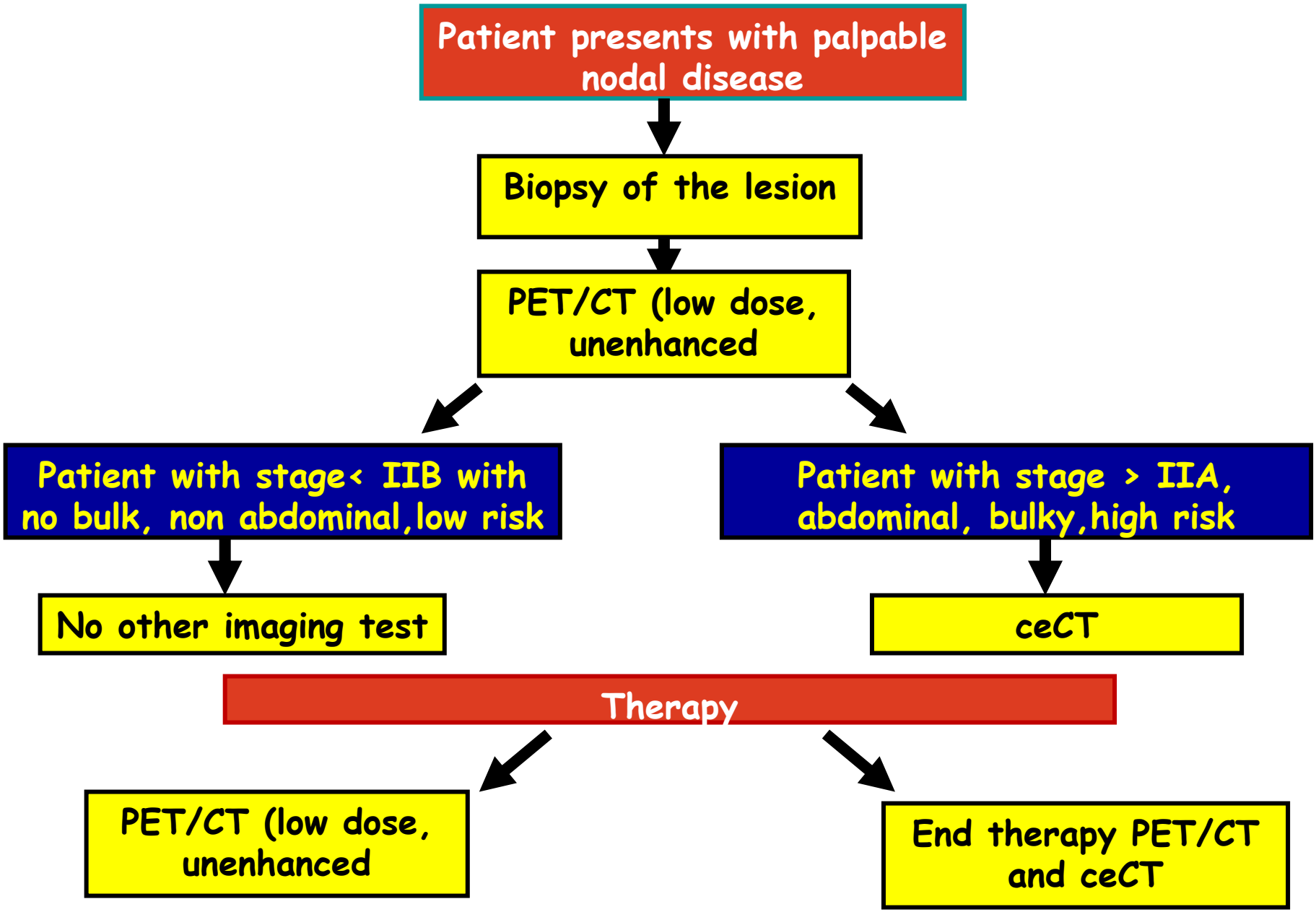
- ceCT or combined PET-ceCT offers adv for,
  - Size measurements for pts who would have a non-CR
  - Abdominal/pelvic lymphoma, END
  - RT planning

- carries an additional radiation burden especially in young HL pts whose cure rates are high

Role of Contrast-Enhanced CT

PET-CT with ceCT is desirable for staging of pts likely to undergo RT ideally within a single scanning session (*category 2*)

A two stage approach using unenhanced PET-CT followed by regional ceCT for equivocal lesions may be preferred taking into account patient age, disease type, bulk and clinical stage


Patient presents with palpable nodal disease
Biopsy of the lesion
PET/CT (low dose, unenhanced
Patient with stage< IIB with no bulk, non abdominal,low risk
Patient with stage > IIA, abdominal, bulky,high risk
No other imaging test
ceCT
Therapy
PET/CT (low dose, unenhanced
End therapy PET/CT and ceCT