XV. ULUSAL MEDİKAL FİZİK KONGRESİ

16 - 19 Mayıs 2015
Karadeniz Teknik Üniversitesi
Osman Turan Kongre Merkezi
Trabzon

Hybrid Tedavi ve Görüntüleme Sistemleri (PET /MR) Nukleer Tip Bakişaçısı

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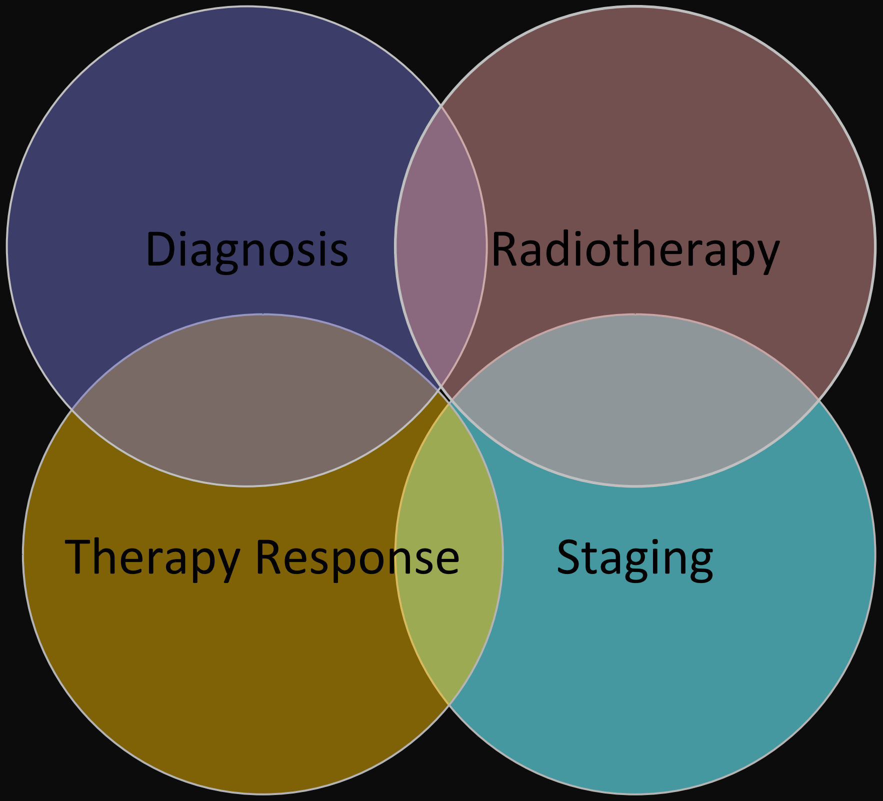
Riyadh, Saudi Arabia

Içerik

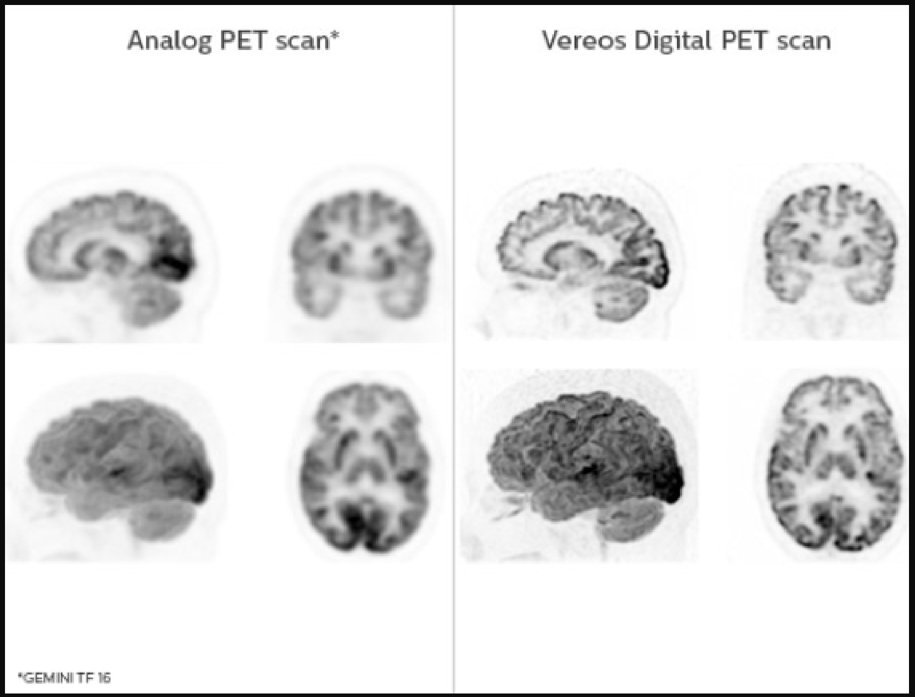
- PET teknolojisindeki radyoterapiyi de etkileyecek son gelişmeler
- PET/MR instrumentasyon
- PET'in radyoterapide kullanimi
- PET/MR: radyoterapi uygulama örnekleri
- PET/MR Sim: Radyoterapi icin gerekli donanım
- Sonuç

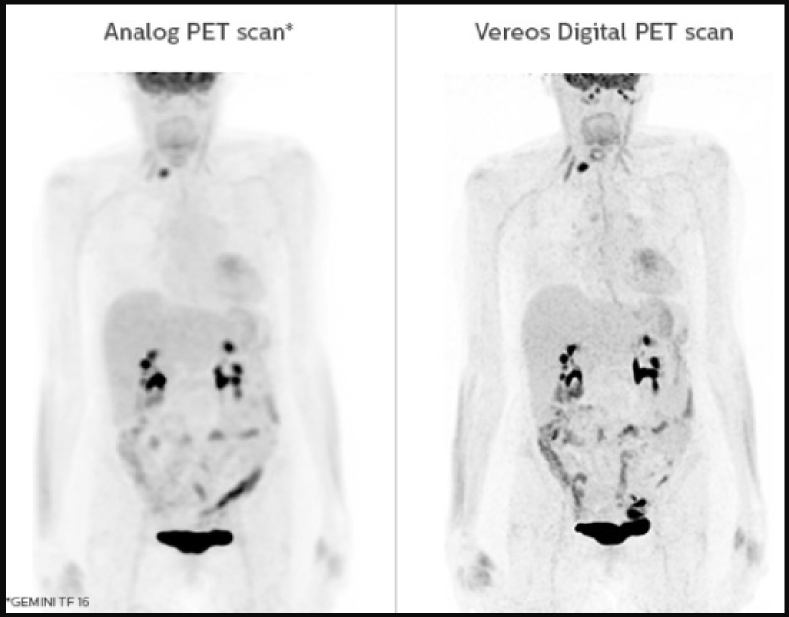
PET teknolojisinde Radyoterapiyi de etkileyecek en son gelişmeler


Diagnosis
Radiotherapy
Therapy Response
Staging

Philips Vereos PET/CT

Digital PET





Uses Photodiodes instead of PMTs

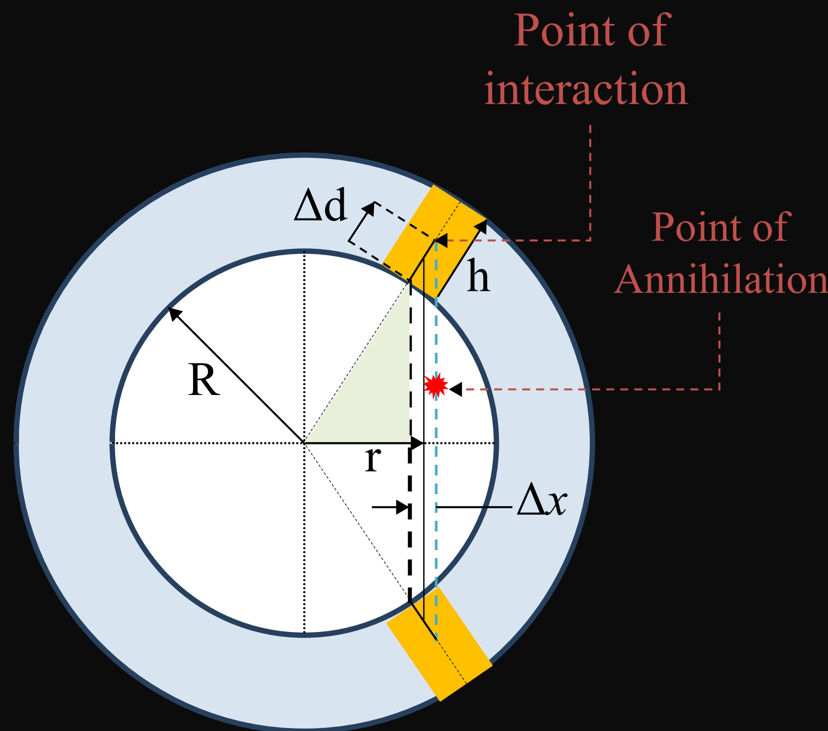
Improves sensitivity (2X) and Volumetric resolution (2x)

Parallax Hatası

Radial resolution blurring

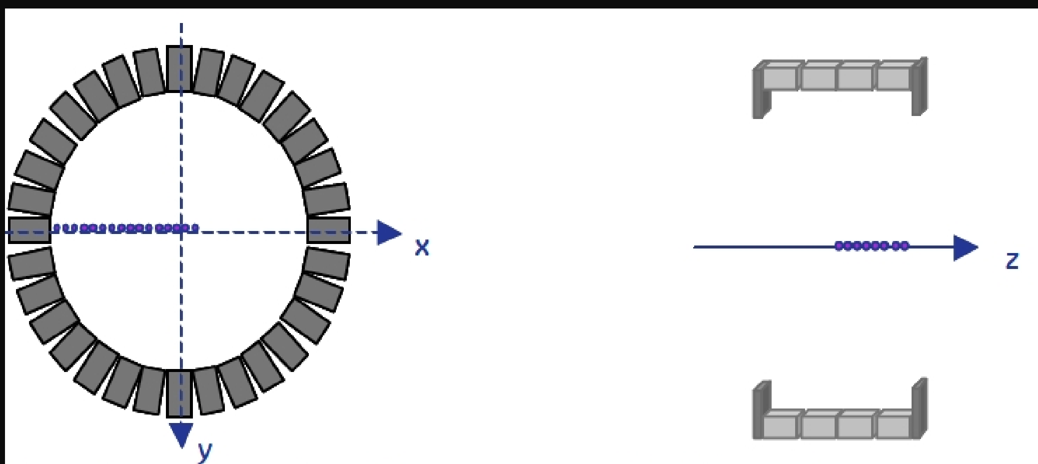
$$\Delta r \approx \frac{r}{\left(D \;\Delta d\right)+1}$$

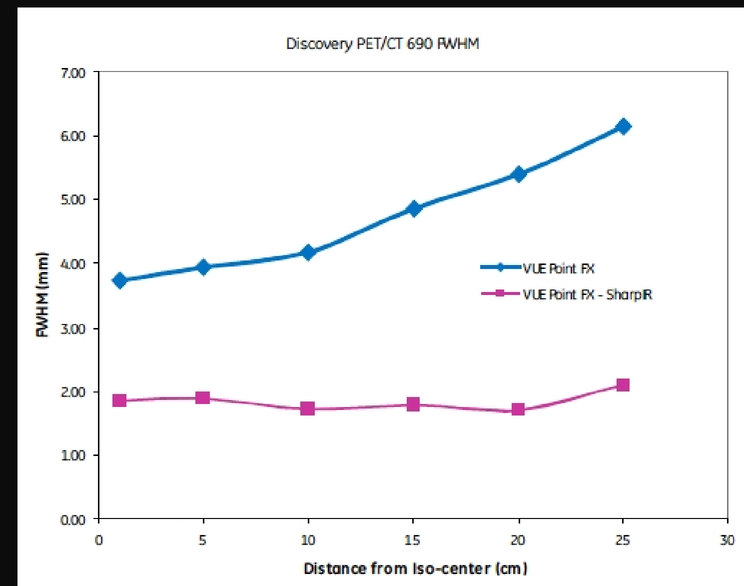
where D is the ring diameter
Δd : interaction depth
r : radial distance



GE Sharp IR

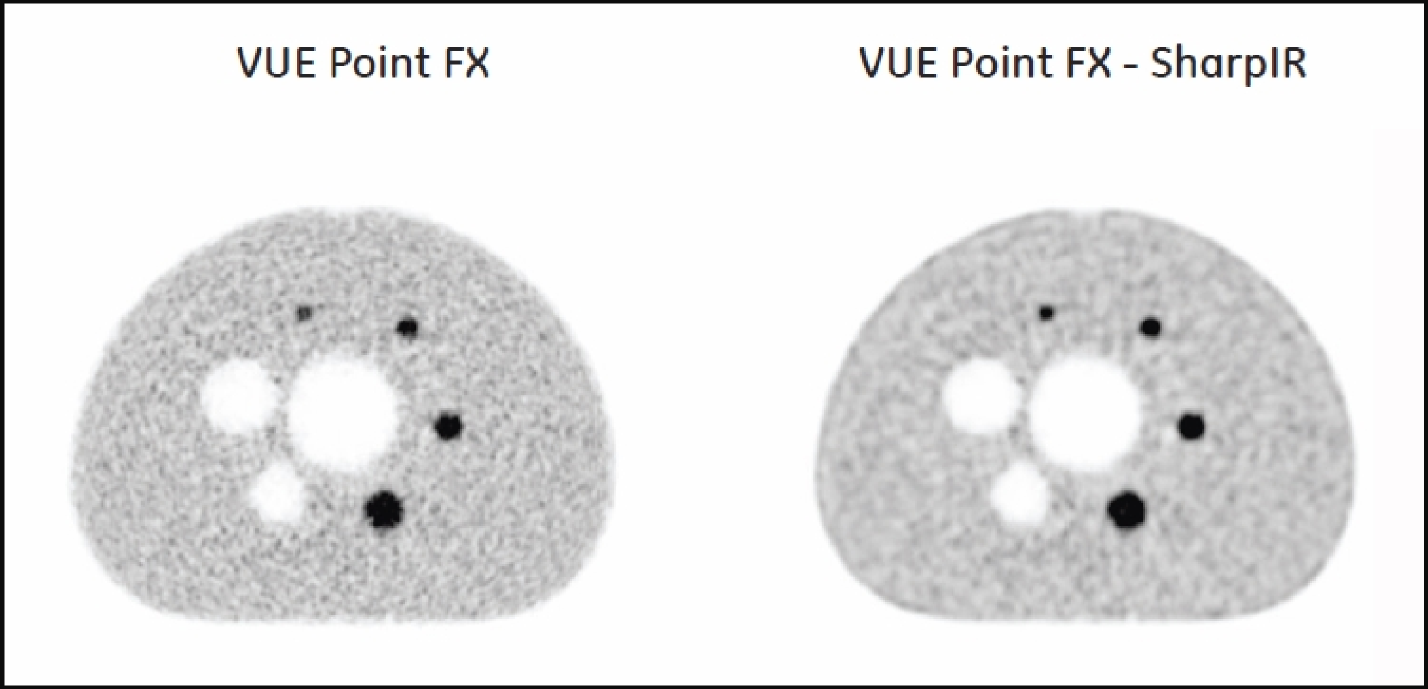
Resolution recovery reconstruction in PET



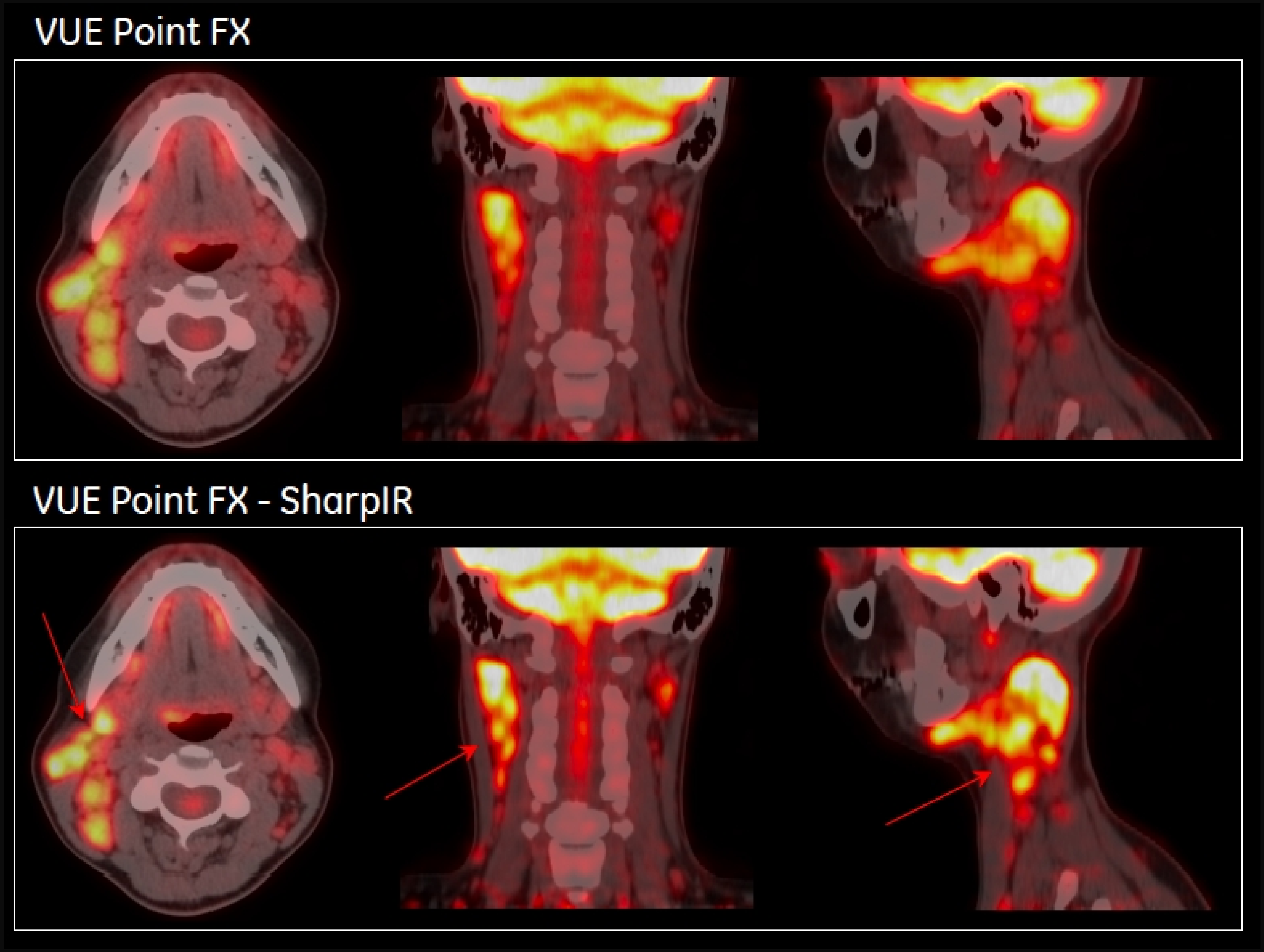


Adam Alessio et al. , IEEE TMI, VOL. 29, NO. 3, MARCH 2010

GE Sharp IR

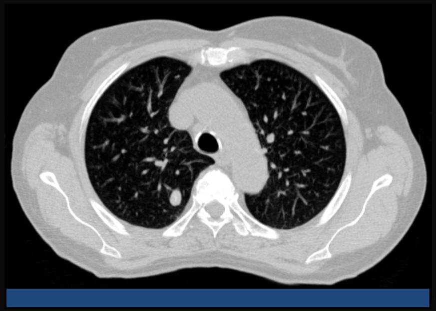


GE Sharp IR

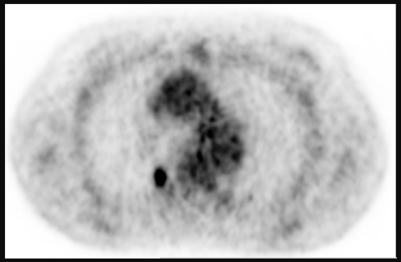


4D Respiratory Gated PET/CT: Planning – Lung Tumor

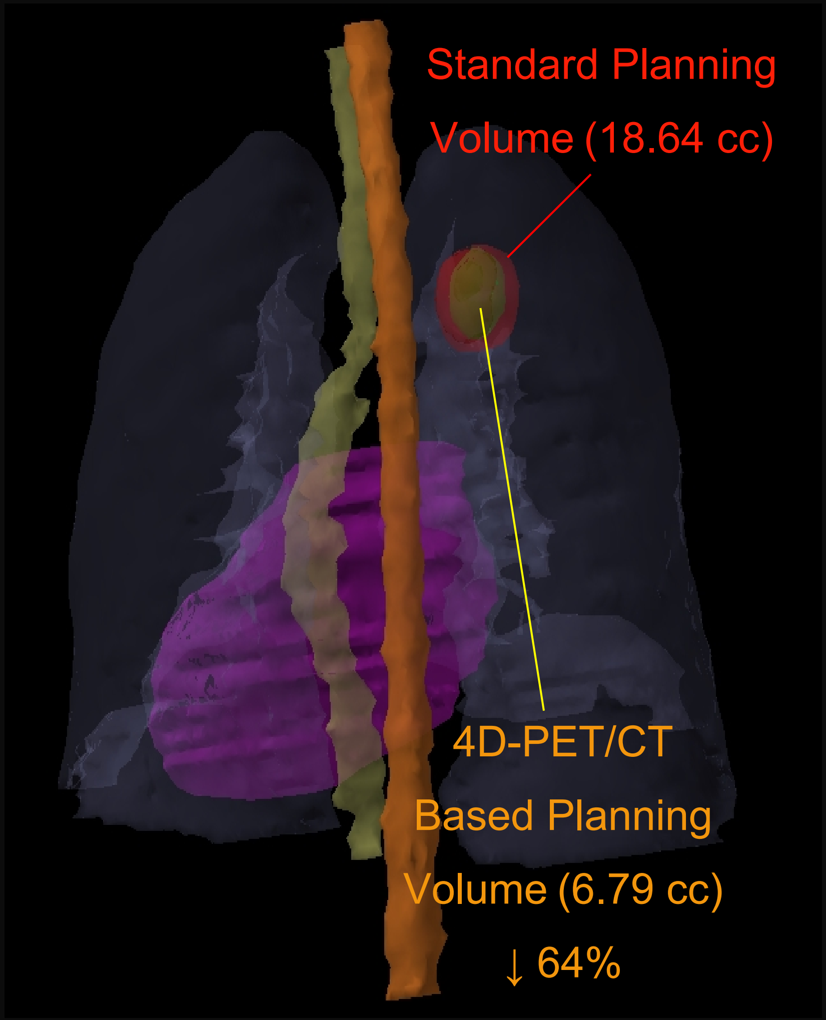
CT



PET

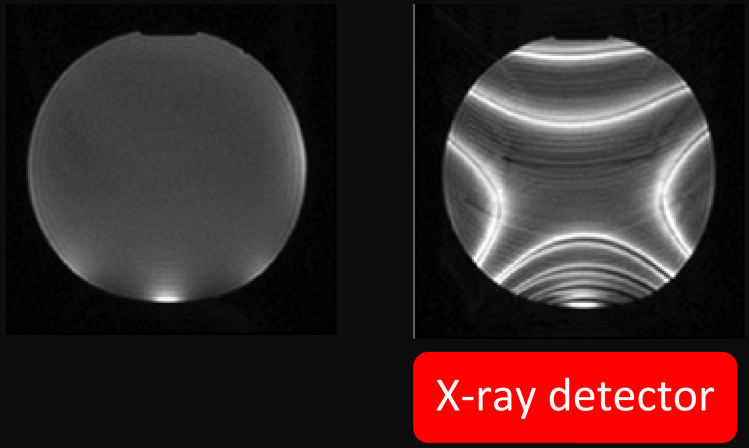


Courtesy
HSR Milan, Italy
Turku PET Centre

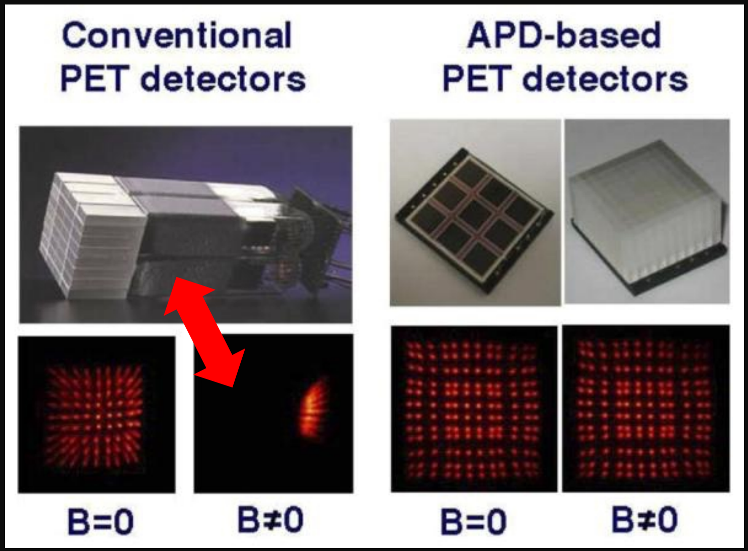


PET/MR İnstrumentasyon

PET ve MRI'ın Entegrasyonu



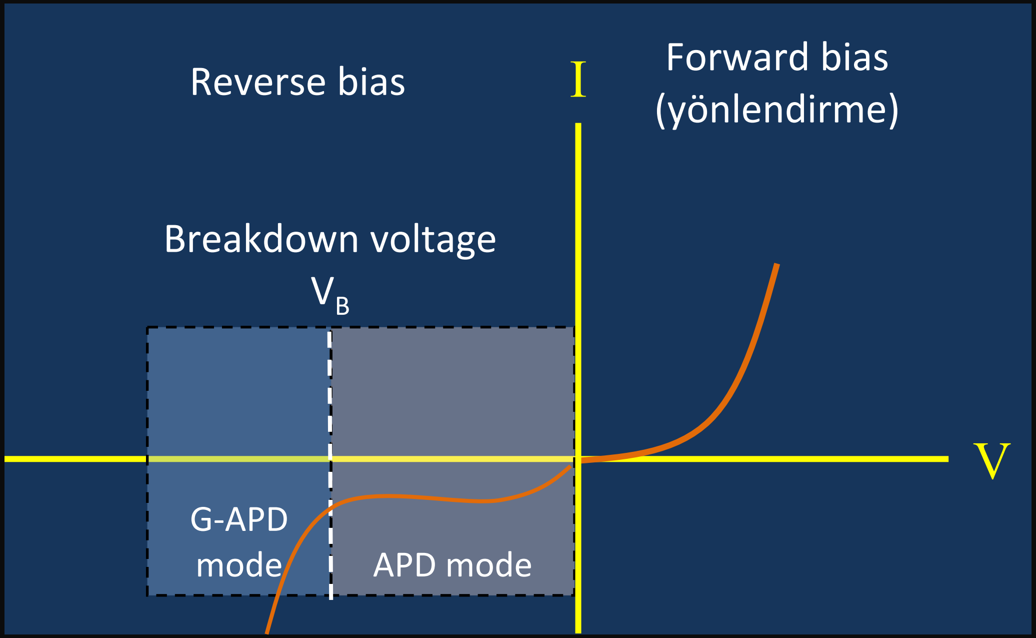
Fahrig, R. et al, *Proceedings of the IEEE* , vol.96, No.3, 2008



Semin Nucl Med. 2008 May; 38(3): 199–208

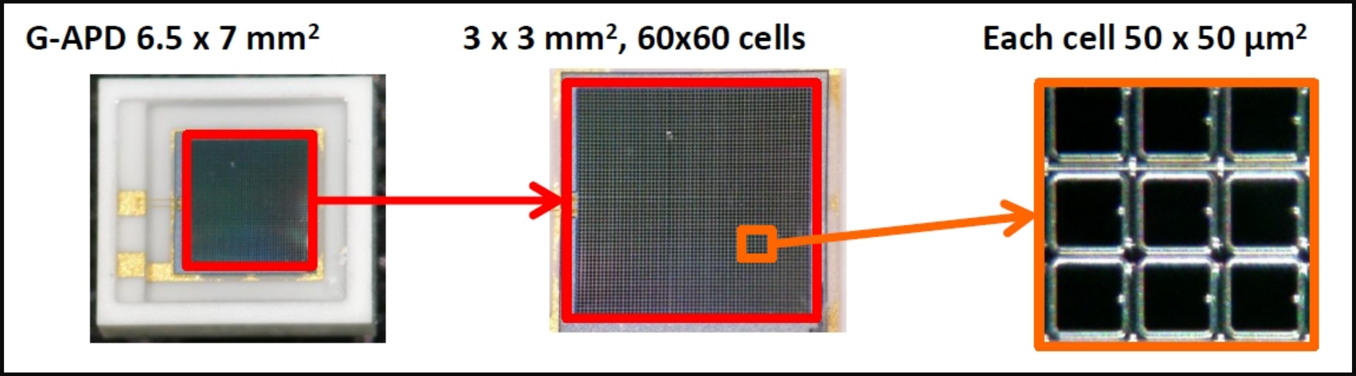
MR Uyumlu Fotodetektörler: APDs ve G-APDs

APD ve Geiger Mode (SiPM)

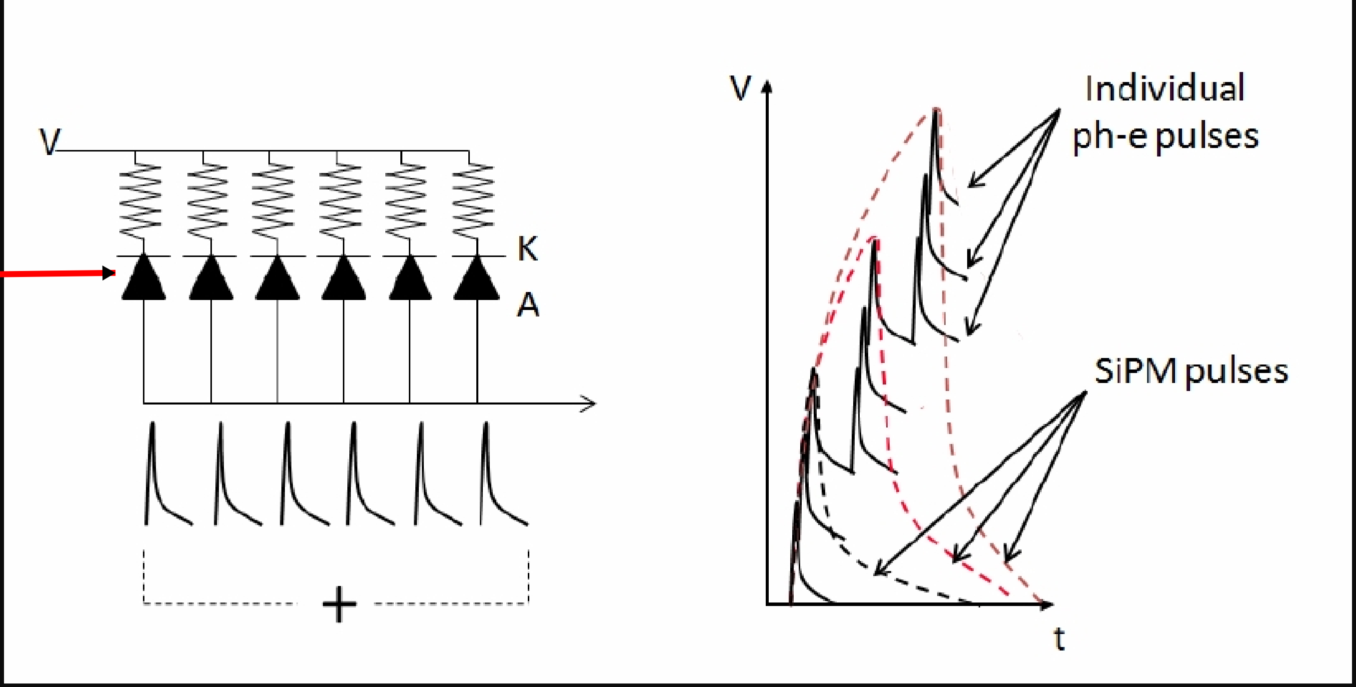


Impact Ionization

SiPM (G-APD, SPAD)



APDs in paralel



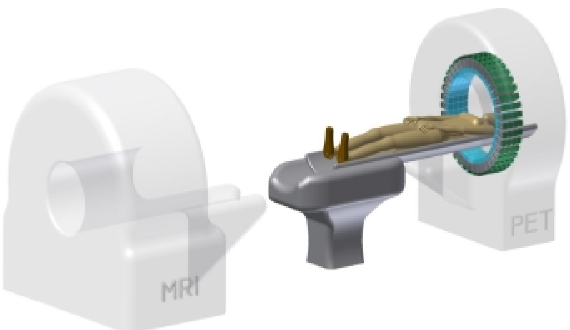
PET/MR'da Kullanilan Fotodetektörler

Photodetector	PMT	APD	SiPM
Detection Efficiency	25%	75%	25%
Yönlendirme Voltajı	1-3 kV	100-500 V	20-80 V
Kazanç	~10^6	50-1000	10^6
Spectral Response	300-550 nm	320-1000nm	320-900 nm
Manyetik alandan etkilenme	Evet	Hayır	Hayır
Time-of-Flight	Evet	Hayır	Evet
Isıdan etkilenme (%/C°)	1	3	1-8
Fiyat/channel ($)	> 200	~100	~50

Sensors, 2010, pp. 10484-10505

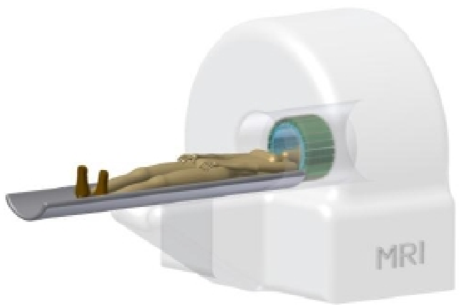
Değişik Dizayn Modelleri

side-by-side



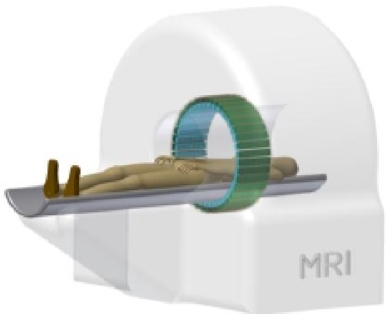
- Use current PMT technology
- Move PET readout away from MR field

PET-insert



- Requires use of MR compatible light detector
- Only modify PET to be transparent to MRI

Integrated PET/MRI



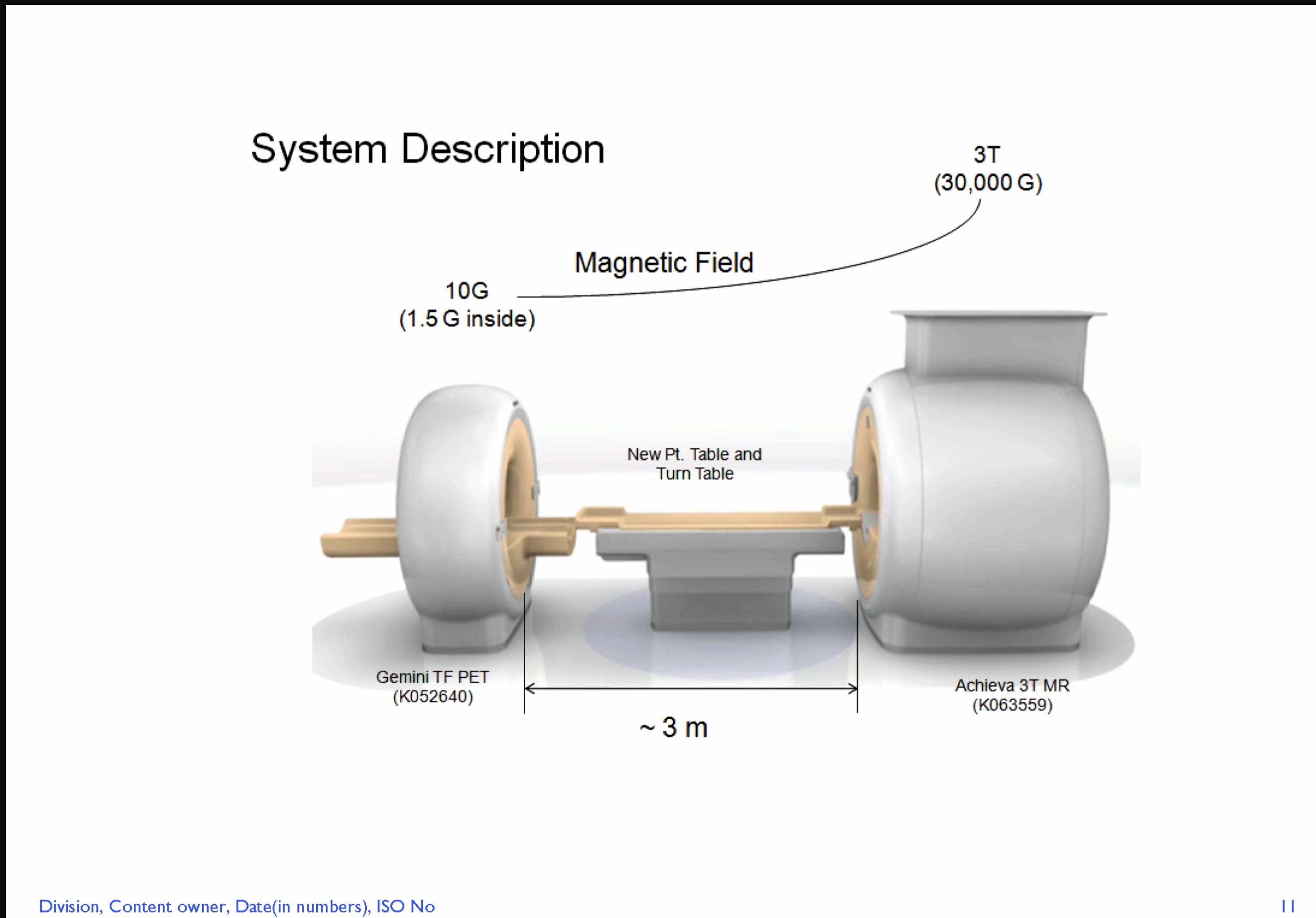
- Merge PET and MRI technology
- Fully integrate PET into the MRI hardware

Slide Courtesy of Martin S. Judenhofer

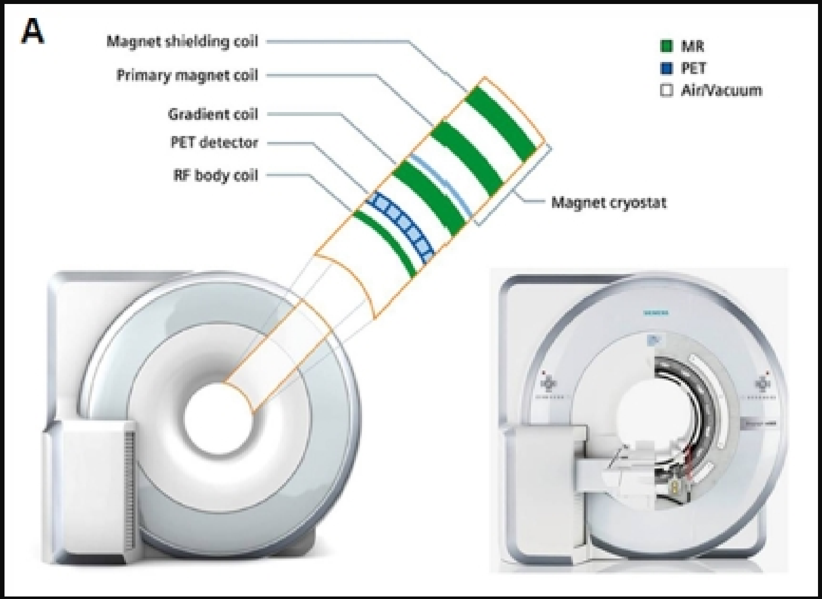
Kilinik PET/MR Sistemler

Uretici Firma ve Model	Philips Gemini TF	Siemens Biograph mMR	GE SIGNA PET/MR
Görüntüleme metodu	Ardışık	Aynı anda	Aynı anda
Kristal	LSO	LYSO	LYSO
FDA Onayi	2011	2011	2014
Fotodetektör	PMT	APD	SiPM
Satilan (sipariş) (Mayis ‘15)			7(10)

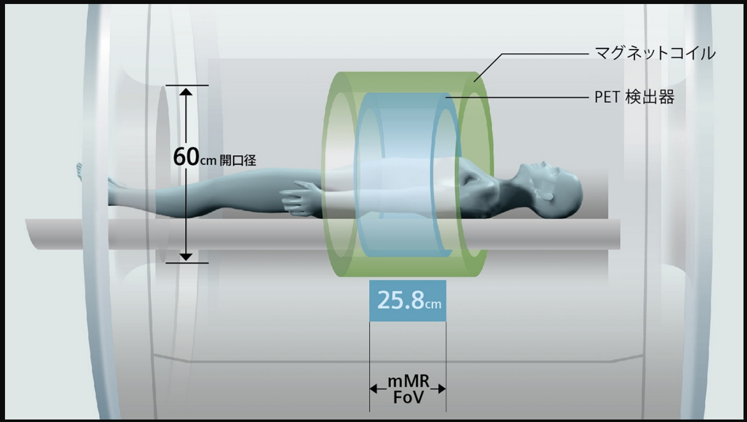
Philips Ingenuity TF & Achieva 3T



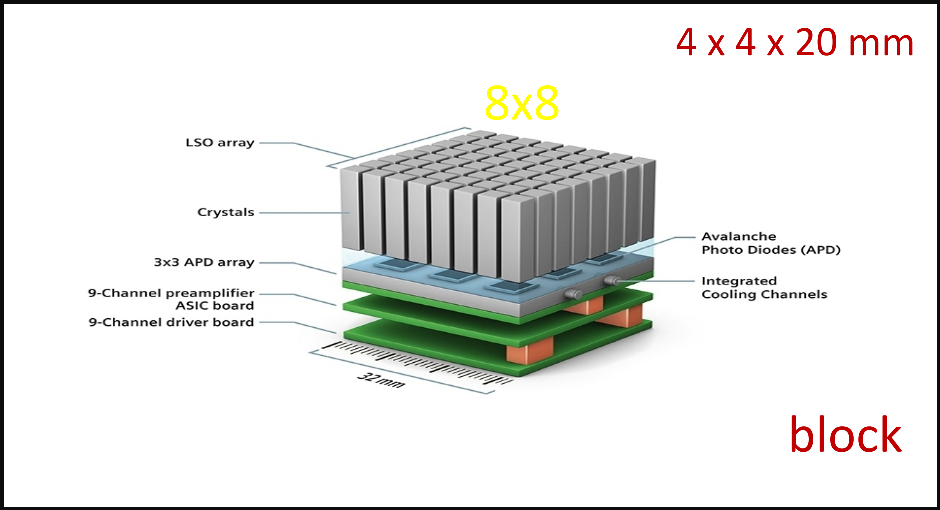
Siemens Biograph mMR



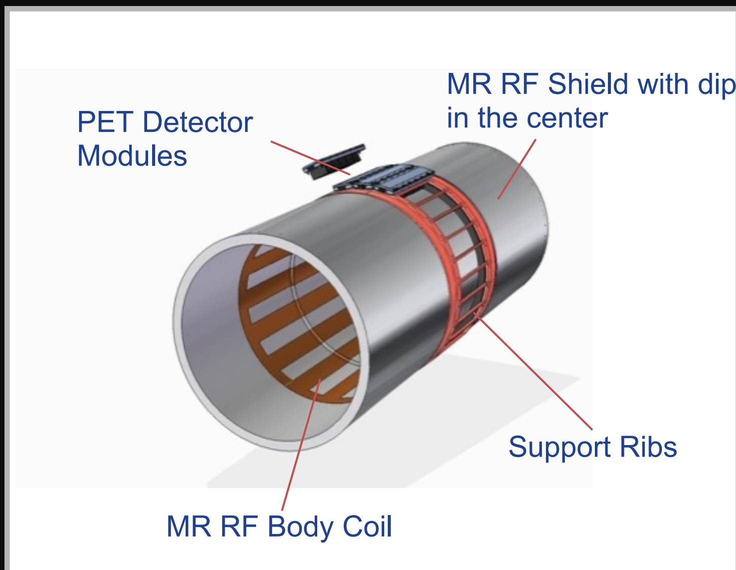
Siemens Broshure (website)



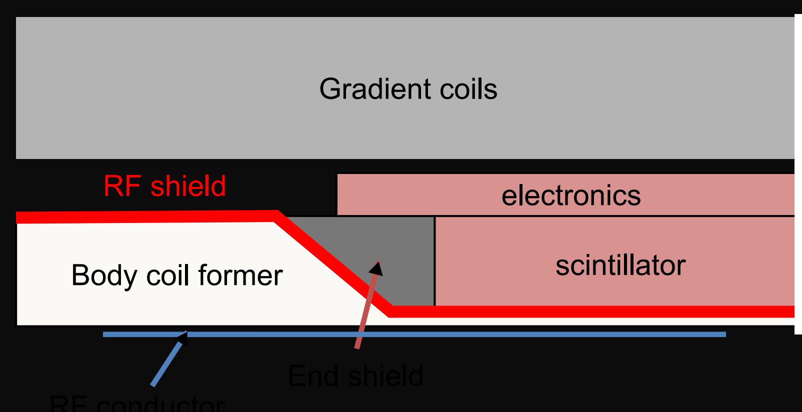
8 Rings of 56 detector blocks



GE SIGNA PET/MR System Design



- PET detector ring mounted between the RF shield and the gradient coil.
- Silicon PhotoMultipliers (SiPMs) for size and magnetic compatibility
- Detectors in ring on outer surface of novel RF body coil – 60 cm bore diameter



Slide Courtesy of Chuck Stern

	GE SIGNA [1]	Siemens Biograph mMR	Philips Ingenuity TF
Trans. FOV	60	59.4	70.7
Sensitivity (kcps/MBq)	21	15	7
Peak NECR (kcps)	210	183.5	90
Energy resolution (%)	11	14.5	12
Timing resolution (ps)	400	2930	520
Axial FOV (cm)	25	25.8	18
Spatial resolution			
Transaxial (@1 cm, 10 cm)	3.7, 4.5 (Iterative)	4.3	4.7, 5.1
Axial (@ 1 cm, 10 cm)	4.8, 4.7	4.3	5
Reconstruction	TOF and PSF	NO TOF and PSF	TOF and PSF

[1] Chuck Stern, GE PET Scientist

UNIVERSITÄTS KLINIKUM TÜBINGEN

EBERHARD KARLS UNIVERSITÄT TÜBINGEN

Navigation

- Tübingen PET/MR Workshop
- Scientific Program
- Registration & Payment
- Location, Transportation & Accommodation
- Social Events
- Endorsements & Sponsoring
- Young Fellow Workshop Stipends

4th Tübingen PET/MR Workshop: February 23 - 27, 2015

Dear Colleagues,

it is our great pleasure to invite you for the fourth time in a row to our PET/MRI workshop in Tübingen. The programme includes ample time for intensive discussions on emerging applications of PET/MRI and its implication in research and clinical practice. We have invited internationally renowned experts from the fields of nuclear medicine, radiology and imaging science to provide a platform for a vital exchange of experiences. As in previous years, round table discussions will target immediate questions in the realms of innovative research, clinical applications, workflow issues and technical challenges linked to this new technology.
The workshop is preceded by a 2-day hands-on course providing training and reading with the expert sessions to small interactive groups. We very much hope that with this programme we can again address a very interdisciplinary audience of clinical experts and imaging advocates to initiate a continuous lively exchange of perspectives, experiences and to foster vivid discussions on the future of PET/MRI.

We are looking forward to welcoming you in Tübingen in February of 2015.

Bernd Pichler, PhD, on behalf of the Organizing Committee

Combined PET/MRI: *Whole-body Multi-Parametric Mapping is Here.* Summary Report of the Fourth International Workshop on PET/MRI Imaging; February 23-27, 2015, Tübingen, Germany

D.L.Bailey, B.J.Pichler, B.Gückel, [xxx] and T.Beyer

on behalf of the discussants and presenters in the following sessions:

Roundtable Discussion: H Barthel, D-M Koh, V Goh, M Schaefers, J Czernin, B Rosen, F Fahey;

Courtesy of Dale Bailey

REVIEW ARTICLE

Combined PET/MR: Where Are We Now? Summary Report of the Second International Workshop on PET/MR Imaging April 8–12, 2013, Tubingen, Germany

Dale L. Bailey,[1] Henryk Barthel,[2] Bettina Beuthin-Baumann,[3] Thomas Beyer,[4] Sotirios Bisdas,[5] Ronald Boellaard,[6] Johannes Czernin,[7] Alexander Drzezga,[8] Ulrike Ernemann,[5] Christiane Franzius,[9] Brigitte Gückel,[10] Rupert Handgretinger,[11] Markus Hartenbach,[12] Dirk Hellwig,[13] Helen Nadel,[14] Stephan G. Nekolla,[15] Thomas Pfluger,[16] Bernd J. Pichler,[17] Harald H. Quick,[18] Osama Sabri,[2] Bernhard Sattler,[2] Jürgen Schäfer,[10] Fritz Schick,[19] Barry A. Siegel,[20] Heinz P. Schlemmer,[21] Nina F. Schwenzer,[10] Jörg van den Hoff,[3,22] Patrick Veit-Haibach,[23] Hans F. Wehrl[17]

REVIEW ARTICLE

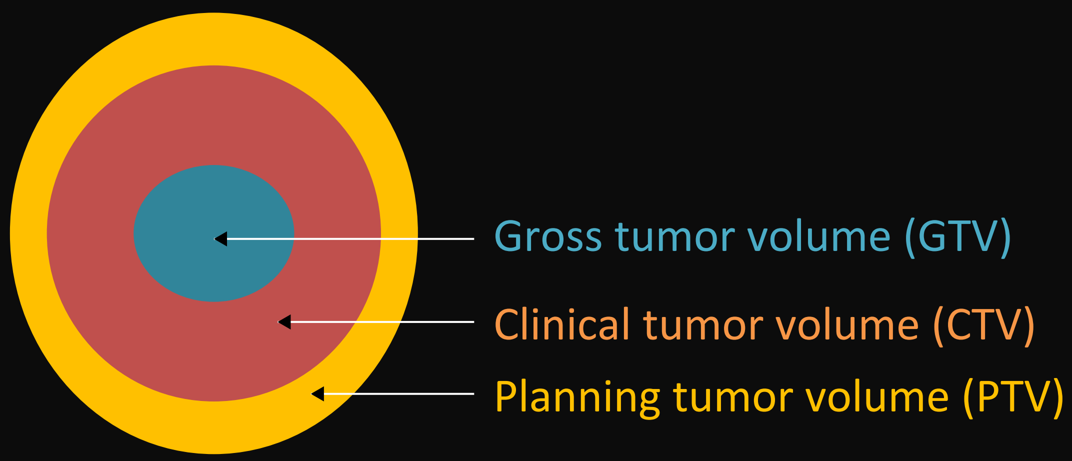
Summary Report of the First International Workshop on PET/MR Imaging, March 19–23, 2012, Tübingen, Germany

Dale L. Bailey,[1] Henryk Barthel,[2] Thomas Beyer,[3] Ronald Boellaard,[4] Brigitte Gückel,[5] Dirk Hellwig,[6] Hans Herzog,[7] Bernd J. Pichler,[8] Harald H. Quick,[9] Osama Sabri,[2] Klaus Scheffler,[10,11] Heinz P. Schlemmer,[12] Nina F. Schwenzer,[5] Hans F. Wehrl[8]

[1]*Department of Nuclear Medicine, Royal North Shore Hospital, Sydney, Australia*
[2]*Department of Nuclear Medicine, University of Leipzig, Leipzig, Germany*
[3]*Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Vienna, Austria*
[4]*Department of Nuclear Medicine and PET Research, VU University Medical Centre Amsterdam, Amsterdam, The Netherlands*
[5]*Department of Diagnostic and Interventional Radiology, Eberhard Karls University Tübingen, Tübingen, Germany*
[6]*Department of Nuclear Medicine, Saarland University Medical Center, Homburg, Saar, Germany*
[7]*Institute of Neuroscience and Medicine-4, Forschungszentrum Jülich, Jülich, Germany*
[8]*Division Werner Siemens Imaging Center, Department of Preclinical Imaging and Radiopharmacy, Eberhard Karls University Tübingen, Tübingen, Germany*
[9]*Institute of Medical Physics, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany*
[10]*Department of Biomedical Magnetic Resonance, Eberhard Karls University Tübingen, Tübingen, Germany*
[11]*DMRC Department, Max Planck Institute for Biological Cybernetics, Tübingen, Germany*
[12]*Department of Radiology, German Cancer Research Center (DKFZ), Heidelberg, Germany*

PET’in Radyoterapiye Kullanımı

PET'in Radyoterapi Kullanimi



- Biolojik tumor hacminin nin belirlenmesinde
- Tumor heterogeneity ve doz boyama

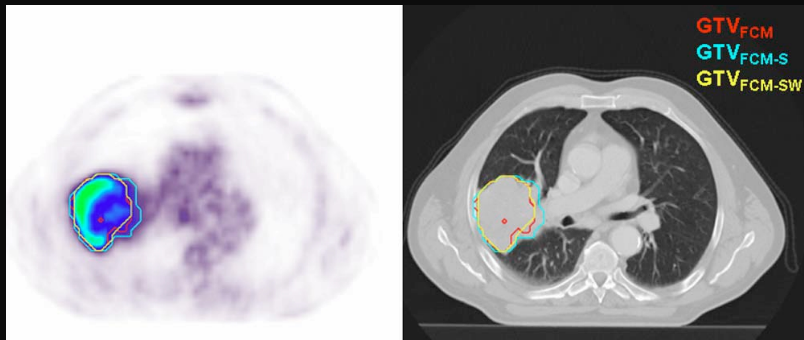
Tumor Segmentation in PET

Segmentasyon	Aciklama	References
Isocontour	SUVmax*(0.36-0.44) 4 mL > tümörler için T/B oranina bağlı	Erdi Y, Mawlawi O, Larson S, et al., 1997;80:2505-2509.
Manuel	Çok yaygın olarak kullanılmakta	
Sabit eşik (threshold)	2.5 veya farklı	Çok yaygın olarak kullanılmakta

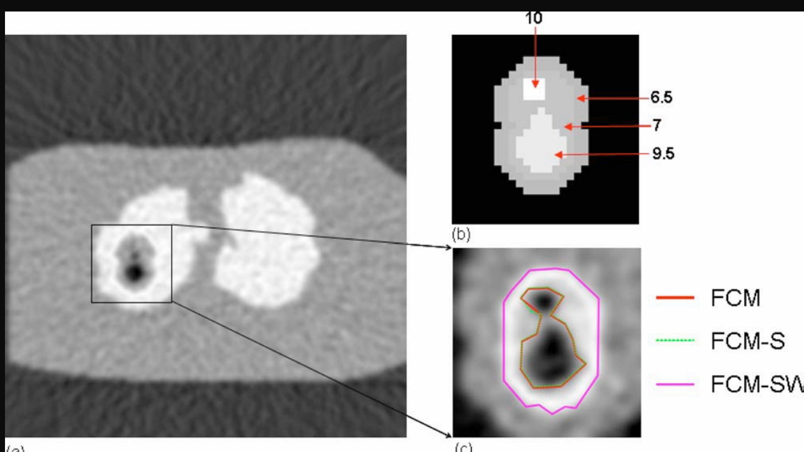
Tumor Segmentation in PET

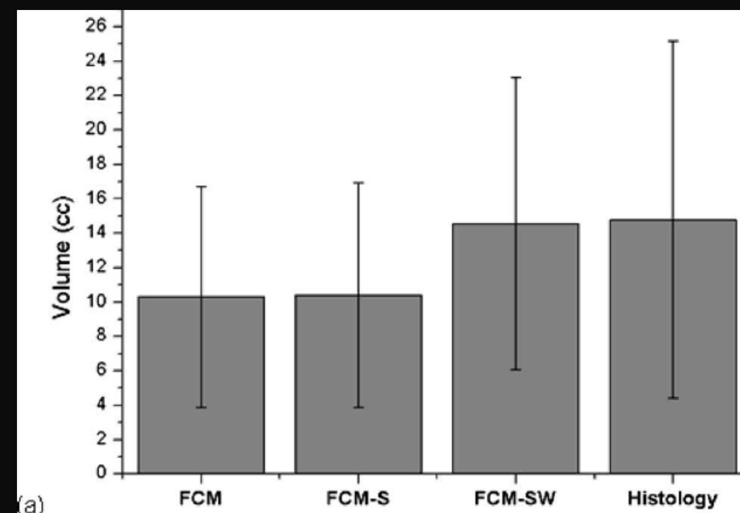
Segmentasyon	Aciklama	References
Background (zemin) tabanlı	Zemin Ortalama + Sabit*Standard Sapma	Percist: 1.5*Liver mean + 2*liver STD 2*Blood Pool in the mediastinum + 2*STD
Fuzzy segmentasyon tabanlı (FLAB ve digerleri)	Pixellerin parlaklık değerine göre yapılır	Hatt M, et al. IEEE TMI. 2009;28(6):881–893
Kenar tabanlı	Gradyan tabanlı	PET Edge MimVista Software
Seeded Region Growing (Bölge büyütme)	Genelde bir tohum pixeli seçilir. Örnegin, SUVmax	Day E, et al. Med Phys. 2009;36(10):4349–4358.

Fuzzy C-Means Algoritması



Araştırmacılar fuzzy c-means algoritmasını anisotropic diffusion ve wavelet transformasyonla beraber kullanmışlar





FCM: Fuzzy C-means
FCM-S: FCM + Anisotropic diffusion
FCM-SW: FCM+ FCM-S + Wavelet

Saoussen Belhassen and Habib Zaidi, Med. Phys. 37 (3), March 2010

Farklı metodları karşılaştıran bir çalışma

25 patients with histologically proven primary NSCLC (Non-Small Cell Lung Cancer

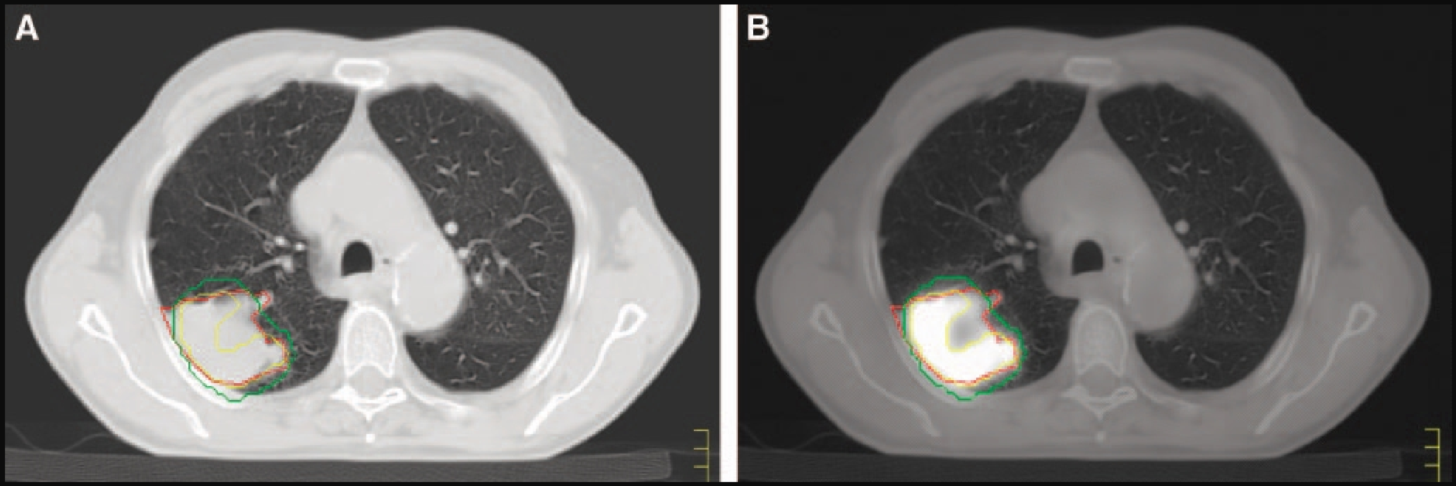
4 methods for GTV

- GTV_{vis}: Visually
- GTV_{40}: 40% of SUV_{max}
- $GTV_{2.5}$: isocontour of SUV = 2.5
- GTV_{bg}: $1.5 * I_{Mean} + I_{background}$
- GTV_{CT}

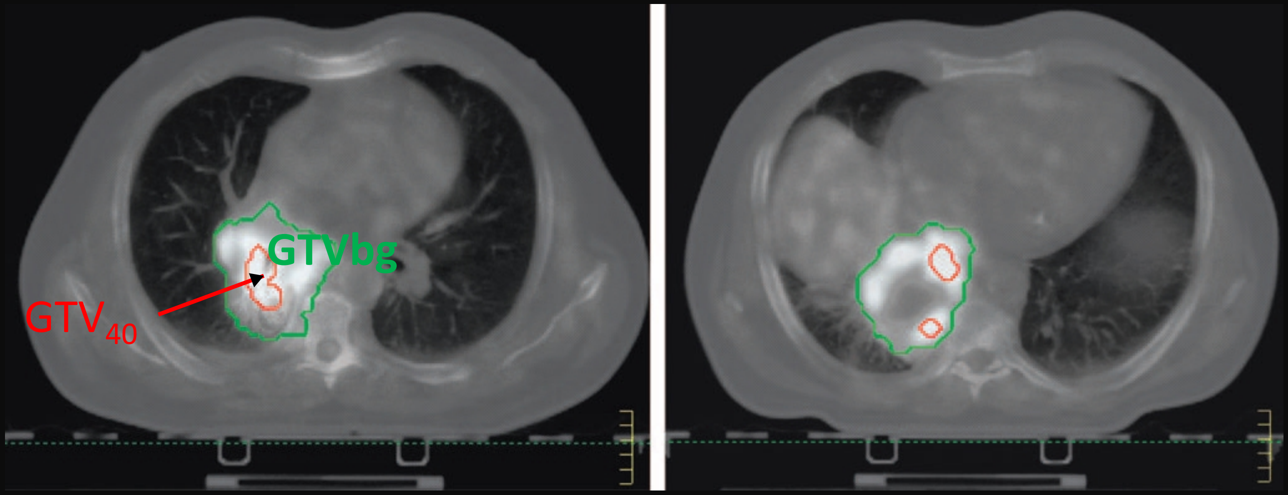
U. Nestle, et al., JNM, Vol. 46, No. 8, Aug 2005

Results and Conclusion

Examples from the Study



Planning CT scan (A) and corresponding fusion image (B) of patient 8 show inadequacy of GTV40: green GTVbg, red GTV_{CT}, yellow GTV_{40}.



PET/CT Radyoterapi

Table 1. Demographic and Clinical Characteristics of 67 Patients.

Patient characteristics	Group A	Group B	Group C	P value*
Patient number	24	22	21	
Gender				
Male	15	14	14	
Female	9	8	7	>0.05
Age (yr)				
Range	19~67	20~68	19~64	
Mean	47	48	46	>0.05
Clinical stages				
III stage	14	13	14	
IVa stage	10	9	7	>0.05
T stage				
T1	1	1	1	
T2	10	9	7	
T3	7	5	9	
T4	6	6	4	>0.05
N stage				
N0	1	1	1	
N1	3	4	3	
N2	15	14	13	
N3	5	3	4	>0.05
Pathologic types				
WHO II	5	4	3	
WHO III	19	18	18	>0.05

*Chi-square test performed.

Group A: conventional chemoradiotherapy group; Group B: CT-guided dose escalation chemoradiotherapy group; Group C: PET/CT-guided dose escalation chemoradiotherapy group; WHO: World Health Organization.

doi:10.1371/journal.pone.0124018.t001

No	GTV_{CT}(cm^3)	$GTV_{PET\text{-}CT}$(cm^3)	Percent of changes(%)
1	15.28	11.09	-27.42
2	7.43	4.12	-44.55
3	10.62	7.57	-28.72
4	30.15	21.72	-27.96
5	15.26	13.05	-14.48
6	32.41	29.27	-9.69
7	15.37	8.66	-43.66
8	44.13	55.17	25.02
9	4.52	2.77	-38.12
10	18.64	13.14	-29.51
11	19.85	14.68	-26.05
12	49.23	54.94	11.60
13	9.46	5.74	-39.32
14	28.31	22.07	-22.04
15	30.68	26.75	-12.81
16	34.16	28.25	-17.50
17	40.42	34.56	-14.50
18	42.15	47.36	11.00
19	22.38	17.34	-22.39
20	55.64	42.34	-23.80
21	31.75	26.42	-16.79

doi:10.1371/journal.pone.0124018.t002

Table 2. The change in GTV volume in Group C patients based on PET/CT.

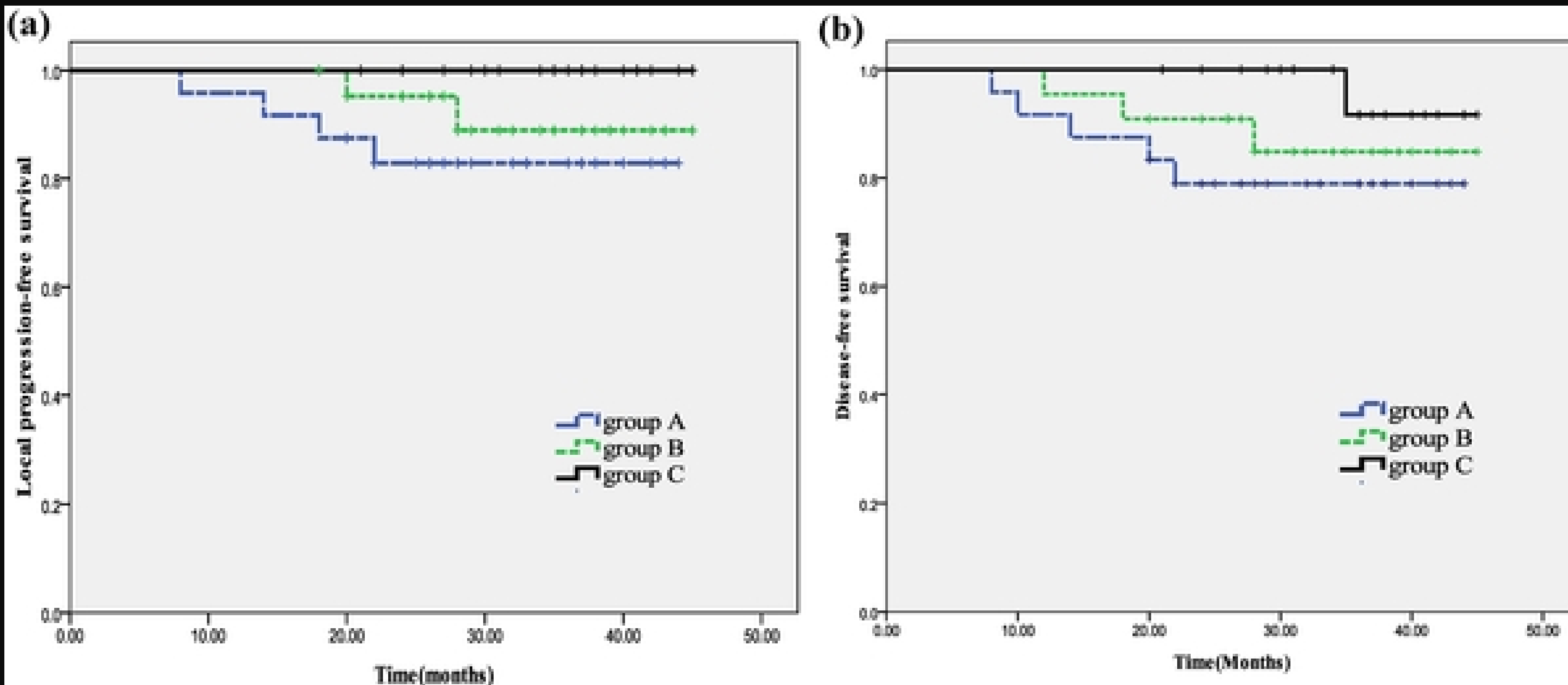
A: Conventional Chemoradiotherapy group

B: CT-guided dose escalation Chemoradiotherapy

C: PET/CT guided dose escelation chemoradiotherapy

Wang J, Zheng J, Tang T, Zhu F, Yao Y, et al. (2015) A Randomized Pilot Trial Comparing Position Emission Tomography (PET)-Guided Dose Escalation Radiotherapy to Conventional Radiotherapy in Chemoradiotherapy Treatment of Locally Advanced Nasopharyngeal Carcinoma. PLoS ONE 10(4): e0124018. doi:10.1371/journal.pone.0124018
http://127.0.0.1:8081/plosone/article?id=info:doi/10.1371/journal.pone.0124018

Fig 2. Kaplan-Meier survival analysis of the treatment groups.



Local Progression Free survival

Wang J, Zheng J, Tang T, Zhu F, Yao Y, et al. (2015) A Randomized Pilot Trial Comparing Position Emission Tomography (PET)-Guided Dose Escalation Radiotherapy to Conventional Radiotherapy in Chemoradiotherapy Treatment of Locally Advanced Nasopharyngeal Carcinoma. PLoS ONE 10(4): e0124018. doi:10.1371/journal.pone.0124018
http://127.0.0.1:8081/plosone/article?id=info:doi/10.1371/journal.pone.0124018

PET/MR'ın Radyoterapi Kullanimi

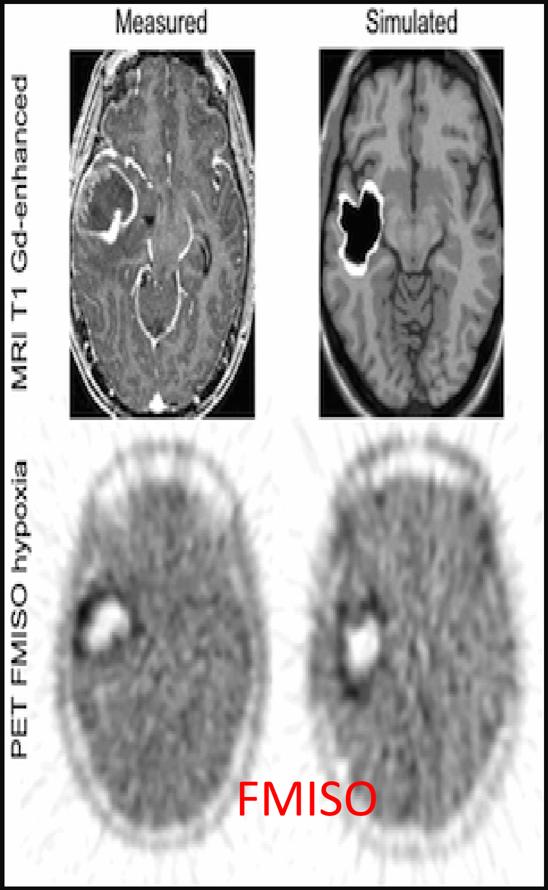
- PET multitracer görüntüleme tekniği
- Tumor sınırlarının belirlenmesinde
- PET deki tumor heterojenliğinin tumorleri daha etkili bir sekilde tedavi etmek icin kullanılması (örneğin, doz boyama (dose painting))
- MR çok parametreli veya çok kontrastlı görüntüleme tekniği
  - Difüzyon, perfizyon, T1, T2, CW, MR Spectral görüntü.....
- PET + MR beraber tümörlerin sinirlarinin belirlenmesinde PET/CT den daha etkili olabilir mi? (1 + 1 = 3)
- Hasta hareketinin belirlenmesinde MR kullanılabilir mi?

PET/MR’ı Radyoterapiye Kullanımı

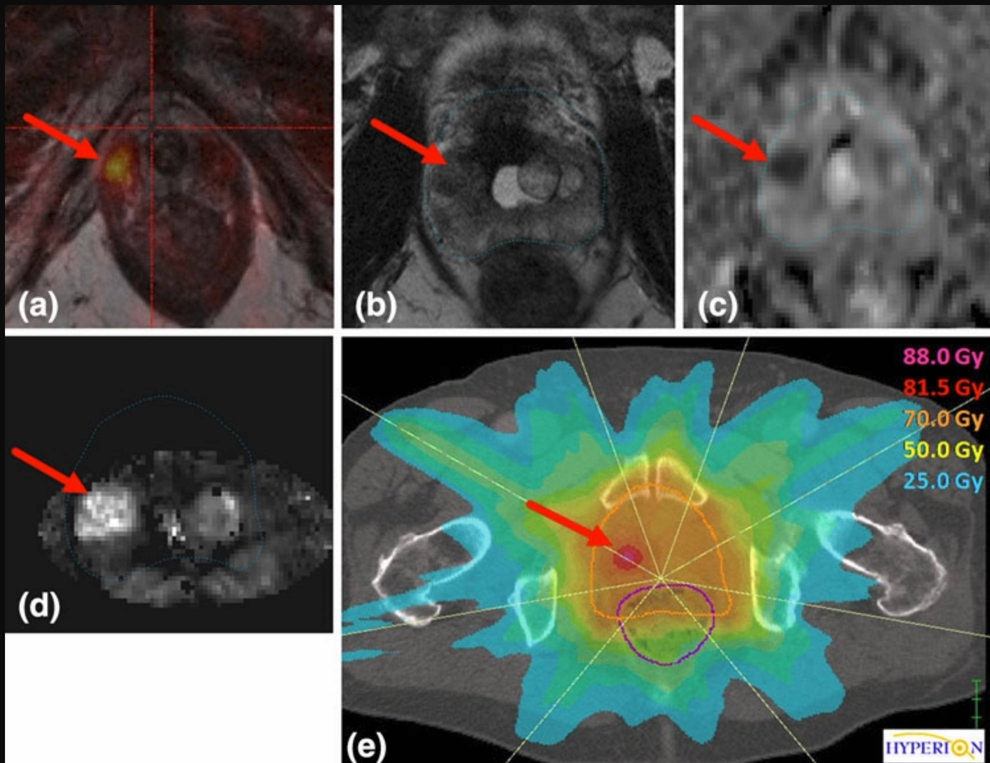
PET/MR'in Radyoterapi Kullanimi

- Hypoxic tümörlerin belirlenmesi veya tumor icinde local hypoxia'nin belirlenmesi

Gu S et al. Math. Med. Biol. 2011



Çok Parametreli Görünteleme ve Doz Boyama



Multi-parametric PET/MRI of a patient with prostate cancer:

(a) Combined [11C]-choline (CHO) PET/MRI
(b) T2-weighted TSE MRI
(c) ADC map derived from DW MRI
(d) Kepmap as a result of DCE-MRI

(e) Dose painting IMRT plan, where a sub-region, on CHO PET, DW- and DCE-MRI, suggesting the presence of the main tumor focus (arrow) was prescribed an escalated dose of 90 Gy instead of 74 Gy, which was prescribed to the whole PTV.
Regions of interest: PTV (orange), rectum (purple).

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Örnek: Sinus Kanseri

Doz escalation yapılabilirmi

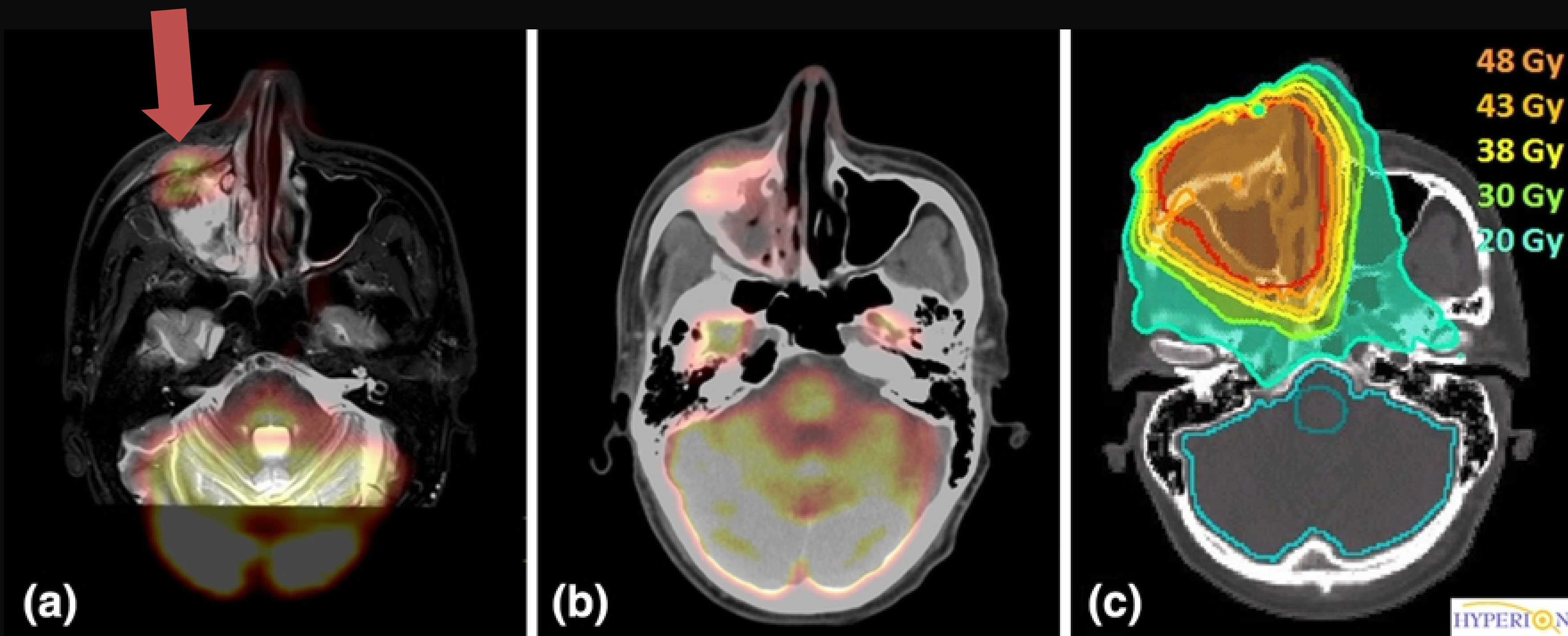

Fig. 2 Simultaneous [18F]-FDG PET/MRI of a 41-year-old patient with sinus cancer (a) and corresponding PET/CT (b). GTV was contoured on both T2-STIR MRI and FDG PET data. IMRT plan with a total dose of 60 Gy to the PTV is shown in (c). Regions of interest: PTV (red), brain stem (dark green), brain (light blue).

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Örnek: Meningioma

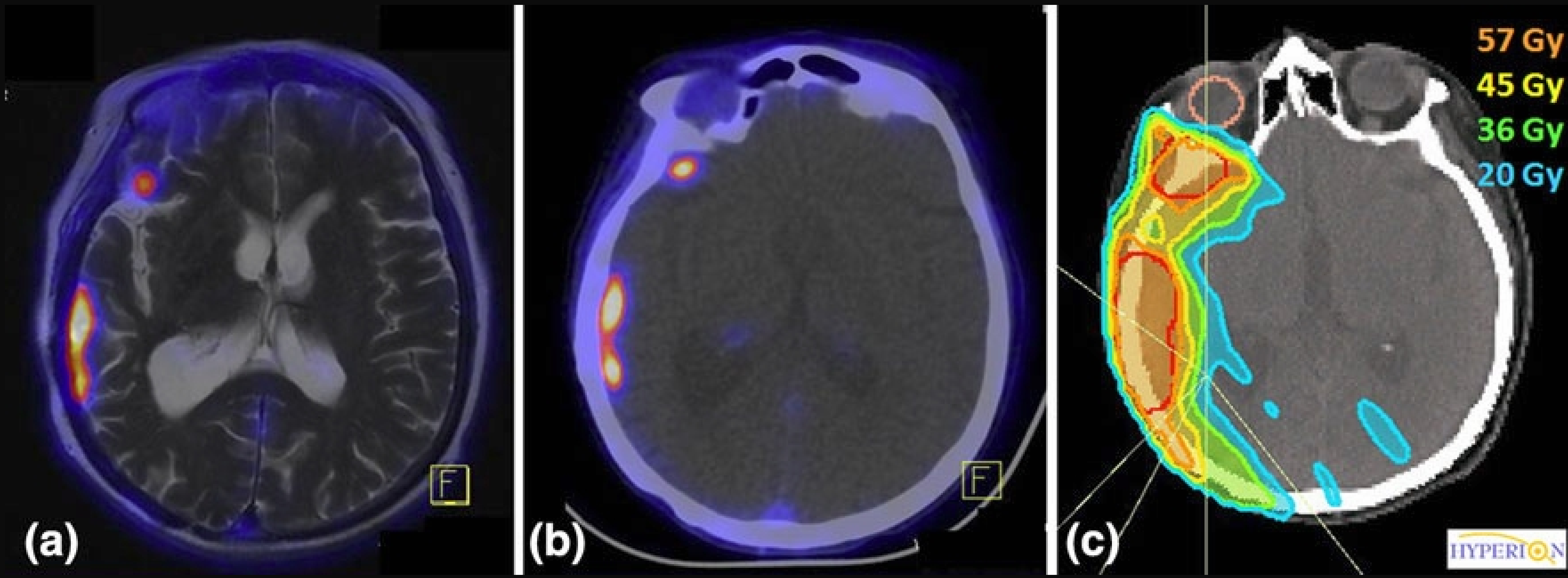

Fig. 1 Combined [68Ga]-DOTATOC PET/MRI (a) and corresponding PET/CT (b) of a 67-year-old meningioma patient. c IMRT treatment plan, where T2-MRI information as well as DOTATOC uptake were used to create the gross target volume (GTV). PET/MRI, PET/CT and planning CT were registered using a rigid image fusion algorithm which is based on mutual information. Planning target volume (PTV, red contour) was prescribed 60 Gy.

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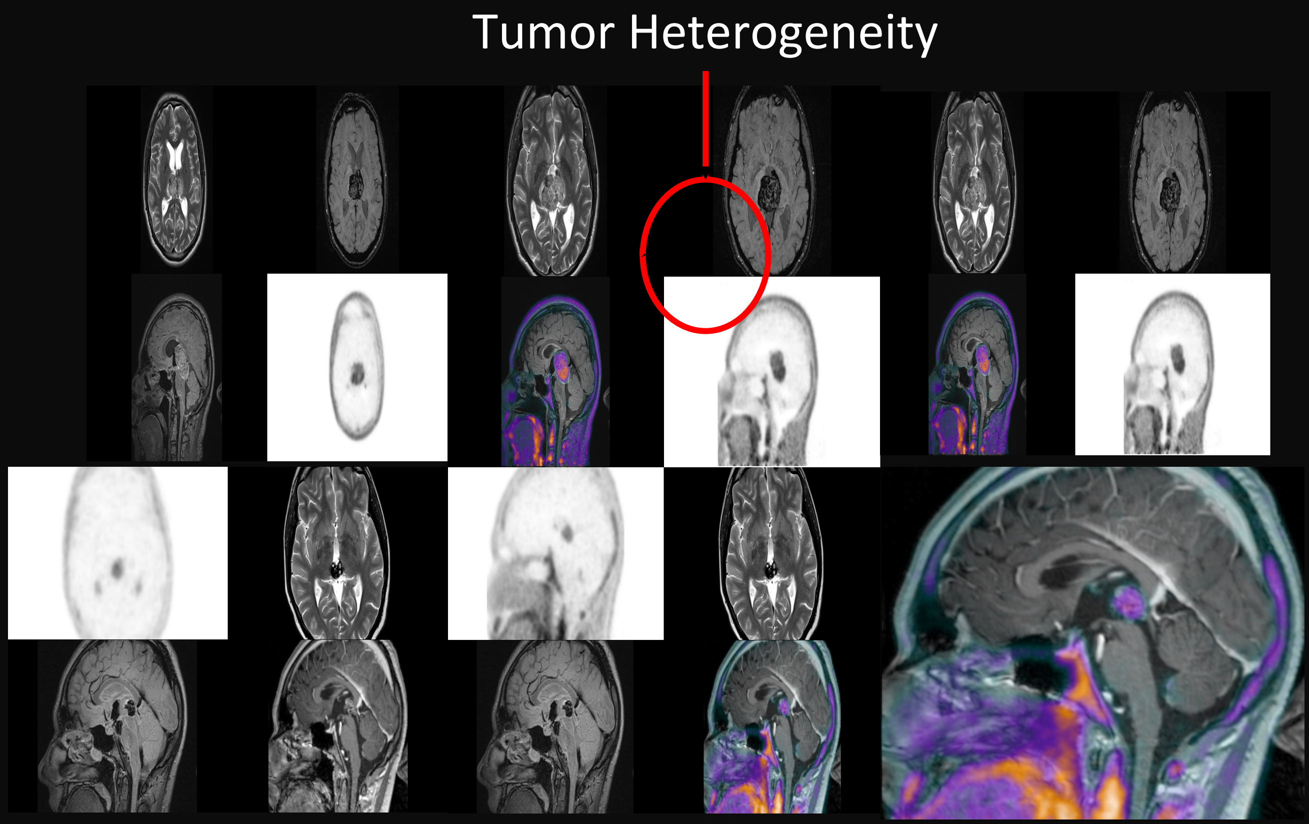
PET/MR'da Tumor Segmentasyon



- Yumusak doku kontrastindan dolayi her iki modalite de otomatik veya yari otomatik segmentasyonda kullanilabilir.
- Tumor heterogeneity etkili tedavi icin cok onemli. Bu konu, uzerinde yeterince calisilmis bir konu degil.

CHOLINE PET/MRI 15yr old pineal tumour, Slide courtesy of Dr. Ridwan Syed

PET/MR Sim veya MR Sim ve Donanim

PET/MRI ve MRI Sim Problemleri Ortak

PET/MRI Sim

Attenuation Map Çıkarılması

Foton azalmasının düzeltilmesi
Scatter fotonlarin düzeltilmesi

MRI Sim

Elektron Density Map

Doz hesaplamalarında

Ikisinin ortak amacı CT olmadan terapi planı yapabilmek

PET/MR Sim

- MR in terapide kullanımı cok daha yeni
- PET/MR in dizaynında karşılaşılan güclükler tamamıyla çözülmüş degildir.
- Bu güçlükler PET/MR Sim'i de etkileyecektir. Bu güçlüklere ek olarak donanım problemleri de vardır.

PET/MR'da Terapi icin Gereken Donanim Ozellikleri

- Düz masaüstü (flat tabletop)

  - Flat tabletopin cok fazla foton azalmasina sebeb olmasi için yeniden dizayn edilmesi gerekir.
  - Carbon fiber dan yapılmış mevcut tabletoplar fazla foton azalımına sebeb olmamaktadır fakat iletkenlik özelliğinden dolayi mevcut magnetik alan, tabletop uzerinde indüksiyon akımları olusturacaktır.
  - Tabletop ların foton azaltma haritaları çıkarılmalı ve normal hasta görüntülerinin üzerine yapıştırılmalı.

- PET/MR sistemlerde bore size yeterince büyük degildir.

- Kullanilan rigid RF coil'lerin de attenuation mapleri çıkarılmalı ve görüntü üzerine yapıştırılmalıdır.

- Hybrid sistemlerde iki gantry uc boyutlu uzayda çakıştırılır. Genelde bu çakıştırmanın doğruluk toleransı diagnostic sistemler icin 5 mm

PET/MR'da Terapi İçin Gereken Donanim Özellikleri

- Hybrid sistemlerde yatak uzun oldugu için yük altında yatak seviyesinde düşme olacaktir. Yine terapi icin kullanilacak sistemlerde bu cökmeden dolayı oluşacak registration hatalari dikkate alınmalıdır..
- Idealde, terapi görüntülerinde voxel boyutlarının izotropik olmasi arzu edilir. Bazi klinik PET/MR sistemlerinde voxel boyutlari isotropic degildir; görüntü kesit kalınlığı farklı ve sabit olabilir.
- MR hasta hareketlerini belirlemek için etkili bir sistem. Eger dokuların haraketlerini karakterize edebilirsek bu bilgi PET reconstruction da kullanilabilir.
- Ayrica PET/MR Sim'de de daha etkili bir terapi icin kullanilabilir.

(a) RT table overlay placed on top of the spine array RF coil on the PET/MR hybrid system.

(b) RF coil holder that is designed to fix the flexible 6-channel body matrix RF coil for RT head/neck imaging.

(c) Mounted RT head/neck imaging setup including the RT table overlay, the RT coil holders, and the body matrix RF coils.

(d) Setup used for the PET evaluation of the RT table overlay.

Sonuç

- PET/MRI'ın radyoterapi de uygulanması çok yeni
- Önce her sistemde donanım problemleri çözülmeli
- PET ve MR bilgilerini kullanacak yeni segmentasyon algoritmalarına gerek var.
  - Mevcut PET bilgisi kullanan algoritmalar MR bilgisini de kullanarak daha etkili hale getirilebilir.
- PET/MR ın terapide daha etkili olabilecegini göstermek icin klinik çok sayıda calismalara ihtiyaç var.
- Bunun için de medikal fizikçiler, onkolojistler ve nukleer tıp doktorları beraber calısmalı.

TESEKKURLER