Incidentne situacije u nuklearno-medicinskoj praksi

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Incidentne situacije su nepredvidive po definiciji ali se potencijalni uzroci mogu u velikoj meri elaborirati i predupredi ti. U cilju osmišljavanja koncepta za klasifikaciju, evaluaciju, sistem kontrole i mere prevencije tokom svih faza nuklearno-medicinskog procesa, uzimajući u obzir i eksterne činioce koji mogu izazvati incidente, definisane su sledeće problemske oblasti: 1) lokalna pravila i procedure; 2) proizvodnja, separacija i aplikacija radiofarmaceutika; 3) radijaciona bezbednost; 4) kontrola kvaliteta nuklearno-medicinske dijagnostičke opreme, kalibratora aktivnosti, prateće IT opreme i uređaja za merenje zračenja; 5) aplikacija i kontrola uređaja i (strukturalnih, ličnih) sredstava za zaštitu od zračenja; 6) problemi pri sakupljanju i skladištenju radioaktivnog otpada; 7) mehaničke povrede (pacijent, zaposleni); 8) greške pri administraciji radiofarmaceutika (pogrešan pacijent, neadekvatna doza, trudnica/dojilja); 9) pacijentov opšti zdravstveni status i 10) uticaj pacijenta u kreaciji, odnosno eskalaciji incidenata. Za praćenje nuklearno-medicinskog procesa, uključujući i eksterne faktore, razvijeno je nekoliko softvera (od kojih su po mišljenju autora najbolji IBC Clinic - Management Process i BioDose/NMIS). Ideja autora je da ovo rešenje za sistematski pristup (potencijalnim) incidentnim situacijama inkorporira u ovim i drugim sličnim softverskim aplikacijama, sa ciljem da ovaj pristup dobije globalni karakter, kako bi se učilo na tuđim greškama i na savremen način, podsticanjem otvorene i jasne razmene informacija, razvijala bezbednosna kultura.

Ključne reči: Nuklearno-medicinska praksa, incidenti, praćenje procesa, softverska aplikacija, bezbednosna kultura.

Manganese Isotopes for Molecular PET/MRI

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Hybrid imaging has become a fundamental tool for diagnostic medicine after the advent of SPECT/PET/CT hybrid tomography. In the last years, a new hybrid system has been introduced combining SPECT/PET with MRI. It should be noted that for all these modalities there is a mismatch between the chemical agents employed for producing the final images. More precisely, SPECT and PET make use of simple radiolabeled molecules for collecting images that possess an intrinsic molecular character, whereas CT and MRI require administration of a bulky amount of contrast agents that essentially yield anatomical images. This suggests that there is a fundamental discrepancy between these imaging approaches deeply rooted in the inherent chemical difference of imaging agents used for PET as compared to contrast agents used for MRI.

We speculated that, for the specific case of PET/MRI, a deeper entanglement between these imaging technologies could be obtained by using exactly *the same* molecule for collecting both PET and MRI images. To accomplish this task, it is first required to identify some element in the periodic table possessing both stable paramagnetic isotopes and radioactive positron emitting radioisotopes. A simple overview reveals that only the elements manganese (Mn) and holmium (Ho) satisfy this condition. In particular, Mn is strongly paramagnetic in the +2 and +3 oxidation states and, concomitantly, it possesses two interesting positron-emitting radioisotopes ^{52}Mn and ^{51}Mn. Thus, Mn could be a suitable candidate for pursuing the scope of achieving a more fundamental molecular fusion of PET and MRI.

Actually, a proof-of-concept for this approach has been already obtained in experiments carried out on animal models where Mn was administered under the simple form of either paramagnetic, Mn^{2+}, and radioactive, $^{52}Mn^{2+}$, ions. In these experiments, Mn^{2+} ions mimic the biological behavior of Ca^{2+} ions that are basically involved in synaptic transmission. Yet this approach is severely limited by the intrinsic toxicity of free Mn^2 ions.

In order to extend the investigation on the diagnostic potential of the combined use of the same molecular imaging agent for PET/MRI, a series of Mn^{2+} complexes were prepared with stable paramagnetic Mn and with the positron emitter ^{52}Mn. Evidence that the paramagnetic and radioactive Mn^{2+} complexes possess the same chemical structure was obtained by spectroscopic and chromatographic methods. Preclinical imaging was carried out in mice with a hybrid PET/MRI scanner.

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PET/CT vs PET/MRI in IBD

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Abstract:
Morphologic imaging, like ultrasound (US), computed tomography (CT) and magnetic resonance (MR) are first line imaging modalities used to evaluate abdominal pathologies. They are available on a large scale, are cost-effective and, in the case of US and MR, they are also radiation-free. However, in some cases, reaching a diagnosis only on the basis of morphologic imaging might be challenging. Nuclear Medicine, being able to evaluate lesion metabolism, can provide important additional information. Nowadays, 18F-FDG PET/CT plays a major role not only in oncologic imaging but also in some infectious and inflammatory disease, such as spondylodiscitis and Inflammatory Bowel Diseases (IBD). Indeed 18F-FDG, as a pan-inflammatory marker, may be useful for the evaluation of diseases activity, for differential diagnosis of fibrotic stenosis vs inflammatory stenosis, and for therapy follow-up.
More recently, PET/MR has emerged as a novel tool to image inflammatory and infectious diseases, with several important advantages over PET/CT:

1. simultaneous acquisition of PET and MR data allows an ideal co-registration and fusion of the metabolic and morphologic data of the entire abdomen, with particular regard to the bowel, which are subject to breathing-induced motion and to peristalsis;
2. higher soft tissue delineation of PET/MR, when compared with PET/CT;
3. lower radiation exposure of PET/MR in relation to PET/CT;
4. complementarity of functional and metabolic investigation trough the addition of diffusion weighted imaging (DWI), and in some cases of magnetic resonance perfusion (MRp), to the 18FFDG PET based investigation of glucose metabolism.

Therefore, PET/MR has the potentiality to replace PET/CT in the infection/inflammatory scenario in the near future.

Keywords: inflammatory bowel disease; 18F-FDG, PET/CT; PET/MR.

FDG PET u Alzheimerovoj demenciji

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Smatra se da demencija zahvata oko jedne desetine gerijatrijske populacije u svetu i skoro polovina obolelih starija je od 85 godina. Sumiranjem epidemioloških podataka došlo se do zaključka da je najčešći oblik demencije Alzheimerova koja predstavlja negde oko 65% svih oblika demencija u starijoj populaciji.

Alzheimerova demencija (AD) karakteriše se prisustvom određenog kliničkog fenotipa u vidu progresivne demencije odnosno gubitka sposobnosti pamćenja koji je ključni simptom, dok se patohistološke promene manifestuju prisustvom intraneuralnih neurofibrilarnih vlakana i esktracelularnih senilnih plakova što je često praćeno sinaptičkim gubitkom i vaskularnim taloženjem amiloda.

Dijagnostički postupci koji se koriste kod AD mogu obuhvatiti različite imidžing modalitete a značajnu ulogu i mesto zauzima pozitronska emisiona tomografija (PET) sa ^{18}F-2-fluoro-2deoksiD-glukoza (^{18}F- FDG).

^{18}F obeležena flurodezoksiglukoza omogućava kvantitativnu ili semikvantitativnu procenu lokalnog metabolizma glukoze u kortikalnim strukturama.

Svaki oblik demencije se karakteriše specifičnom regionalnom distribucijom ^{18}F-FDG unutar velikomoždane kore i time je omogućeno postavljanje dijagnoze odnosno eventualne diferencijalne dijagnoze različitih oblika demencije. Kod demencije Alzheimerovog tipa smanjen metabolizam glukoze zapaža se u posteriornom delu i to najčešće u parijetalnim, superiornim i posteriornim temporalnim regijama. Izmenjena slika regionalnog metabolizma glukoze povezana je sa kognitivnim deficitom i poremećajima ponašanja koji se javljaju u demenciji.

^{18}F-FDG PET kao dijagnostička metoda pokazuje visoku senzitivnost i izuzetno visoku specifičnost u dijagnostici AD, kao i visok stepen pozitivne prediktivne vrednosti u ranoj dijagnostici AD.

Ključne reči: Alzheimerova demencija, FDG PET, kortikalni metabolizam glukoze.

PET/CT vs MRI vs radiolabelled WBC in diabetic foot infections

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Diabetic foot (DF) is a clinical entity characterized by hard to heal ulcers with a very high rate of relapses responsible for a very high risk of major amputation. Diagnosing DF complications is still a challenge since it is not always easy to achieve a precise discrimination between osteomyelitis (OM), soft tissue infection (STI), and Charcot osteoarthropaty. A precise differential diagnosis between these entities is of pivotal importance in order to ensure an adequate treatment to the patients.

Radiolabelled WBCs scintigraphy is nowadays a well-consolidated modality that allows detecting infections with high sensitivity, specificity and diagnostic accuracy. However, a major limitation of planar images is represented by the lack of anatomical landmarks that could affect the exact localization of the infection. The use of SPECT/CT in addition to planar images could overcome this limitation and could be useful to evaluate the extent of the infective process, thus further improving the accuracy of radiolabelled WBCs.

On the other hand PET/CT offers several advantages over conventional scintigraphy: first of all it avoids the manipulation of potentially infected blood, secondly the acquisition time is considerably shorter than radiolabelled WBC, thirdly images quality resolution is better than planar scintigraphy. Moreover in presence of CT co-registration it is possible to have a precise definition of the anatomical landmarks. Nevertheless, FDG is a non-specific radiopharmaceutical because it accumulates in infections, inflammations, malignancies, reparative processes and in all the other conditions in which the glucose is metabolized as a source of energy. Therefore it is not able to achieve a differential diagnosis between the different features that compose DF. The PET/MRI is emerging as a powerful diagnostic tool for several indications in the field of infection and inflammation. At present no studies exploring the utility of this modality in this specific clinical setting are available but, considering the high quality resolution of the images especially for the evaluation of soft tissues, this modality promise to become an undeniable tool also for the assessment of DF disorders.

PET SIMPOZIJUM

PERKUTANE INTERVENCIJE NA HEPATOBILIJARNOM TRAKTU

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Jetra je organ koji neretko biva zahvaćen patološkim procesima, bilo da su oni primarno nastali u njoj ili je ona sekundarno invadirana. Zbog svoje specifičnosti u vaskularizaciji, strukturi parenhima i sposobnosti da se regeneriše jetra je organ na kome se izvodi možda i najveći broj interventno radioloških procedura. Ili se to nama, koji se ovim poslom svakodnevno bavimo, samo tako čini.

Sve intervencije koje se na jetri izvode mogu se razvrstati na one koje se izvode na parenhimu, vaskularnim strukturama i bilijarnom traktu. U Odseku Interventne radiologije Centra za radiologiju i MR KCS-a godišnje se izvede oko 1000 interventnih procedura na ovom sistemu. Najveći broj na bilijarnom stablu (perkutane bilijarne drenaže, balon kateterske dilatacije, postavljanje kateterskih i metalnih proteza). Na drugom mestu po učestalosti su interventne procedure na parenhimu (perkutane biopsije, sklerozacije i termalne ablacije), a na trećem vaskularne intervencije (TACE, TIPS, PVE).

U ovom radu biće razmatrani različiti aspekti primene svih ovih procedura.

Ekspanzija novih metoda, pojava novih materijala kao i modifikacija postojećih tehnika učinili su da je uspešnost u izvođenju ovih procedura postala značajno veća, a procenat komplikacija značajno manji.

FDG PET/CT application in Sarcoidosis

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Sarcoidosis is defined as a multisystem granulomatous disorder of unknown cause. The pathologic hallmark of sarcoidosis is a noncaseating granuloma consisting of epithelioid and multinucleated giant cells, as a result of inflammation mediated by Th1 lymphocytes. Noninvasive assessment of the granulomatous inflammatory activity and of the extent of chronic sarcoidosis remains a challenge. The serum level of angiotensin-converting enzyme (ACE) produced by sarcoid granulomas is commonly used for evaluation and planning of treatment. However, the ACE level is above the normal limits in only about 60% of patients with chronic sarcoidosis and unrelated to the disease severity, progression, clinical course, and response to therapy. Routine diagnostic procedures, such as chest radiography and multidetector CT (MDCT), are useful for the detection andstaging of pulmonary sarcoidosis, but are unable to reveal active inflammation. The nuclear medicine technique, such as 67-gallium (Ga-67) scintigraphy has also been used for diagnosis and evaluation of the extent of disease. Nowadays, however, it plays a limited role. Integrated PET and CT (PET/CT) with a glucose analogue FDG (FDG-PET/CT) has been increasingly used for the assessment of infectious and inflammatory diseases, including sarcoidosis.

The objective of this review is to highlight the clinical utility of FDG-PET/CT for evaluation of patients with chronic sarcoidosis. It is based on our own experience and literature data. Since 2009, we have performed almost 300 FDG-PET/CT studies for evaluation of patients with chronic sarcoidosis and published 8 papers in the leading nuclear medicine per review journals such as Journal of Nuclear Medicine, Clinical Nuclear Medicine, Seminars in Nuclear Medicine. The emphasis of this review was on the potential advantages and disadvantages of this technique in these patients based on which recommendations were made. The advantage of FDG-PET/CT technique is that it can visualize FDG accumulation in activated inflammatory cells and simultaneously provide PET and CT images. Of particular interest is the use of FDG-PET/CT for the staging and identification of occult sites and sites suitable for biopsy and for the assessment of inflammatory active sarcoidosis in patients with prolonged symptoms, especially when other markers of the disease are within normal values. FDG-PET/CT also provides a better visualization of extrathoracic sites of active sarcoidosis, such as in the bones, liver, spleen, and retroperitoneal lymph nodes. The use of FDG-PET/CT is of special interest in cardiac sarcoidosis because this potentially life-threatening disease is sometimes present in asymptomatic patients. FDG-PET/CT also has a role in the clinical management of patients with chronic persistent sarcoidosis, such as for planning treatment, monitoring response, and long-term follow-up. The limitations of FDGPET/CT in patients with sarcoidosis are discussed in the context of a

“sarcoidosis-lymphoma syndrome” and potentially excessive radiation exposure. Further prospective multicentre studies are needed to refine the clinical applications of FDG-PET/CT in patients with sarcoidosis and drive the field forward.

Priprema bolesnika i metodologija snimanja za PET/CT ispitivanja

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Abstract: Pozitronska emisiona tomografija (PET) je dijagnostička metoda u nuklearnoj medicini za dobijanje slike metaboličke (funkcionalne) aktivnosti u određenim delovima tela. 2-^{18}F-fluoro2deoksiglukoza (^{18}F-FDG), obeležena pozitronskim radionuklidom fluorom-18 (^{18}F) sa vremenom polu-raspada od 109,8 min, predstavlja najčešće korišćeni pozitronski radiofarmak. To je analog glukoze, što mu omogućava da se ponaša kao glukoza pa se olakšanom difuzijom prenosi u ćeliju, posredstvom GLUT transportera (pre svega GLUT1 i GLUT3). U ćeliji se ^{18}F-FDG fosforiliše kao i glukoza heksokinazom kao prvim korakom ka glikolizi. Normalno jednom fosforilisana glukoza nastavlja svoj glikolitički put za proizvodnju energije dok ^{18}F FDG ne može ući u glikolizu i postaje zarobljen intracelularno kao FDG-6-fosfat. U malignitetima, granulomatoznim zapaljenjima i infekcijama imamo povećanu potrošnju glukoze, samim tim i veću akumulaciju ^{18}F-

FDG. Kombinovani PET/CT uređaji pružaju i informacije o metabolizmu glukoze (iz PET studije) i anatomske informacije (iz CT-a) u jednom pregledu. ^{18}F-FDG PET/CT je, iako visokosenzitivna dijagnostička metoda, ipak ograničen nešto nižom specifičnošću i nemogućnošću da jasno razlikuje granulomatozne i inflamatorne bolesti od malignih. Uprkos tome, FDG je skoro idealni trejser za PET primenu u onkologiji. Osim u onkologiji FDG PET/CT ima primenu u ispitivanju kardioloških, neuroloških i inflamatornih oboljenja.

Priprema za PET/CT snimanje počinje otprilike jedan dan pre zakazanog PET/CT ispitivanja. Cilj pripreme pacijenta za ^{18}F-FDG PET/CT je da minimizira kompetitivnu inhibiciju unosa ^{18}F-FDG u ćelije povezane sa glukozom i da smanji nivo insulina u serumu do bazalnog nivoa. Pored toga, važno je takođe minimizirati unos radiofarmaka u zdrava tkiva, kao što je miokard i skeletni mišić, uz održavanje unosa u ciljnim tkivima. Zbog toga se preporučuje dijeta siromašna ugljenim hidratima a sa visokim sadržajem proteina i/ili masti (posebno ukoliko je ciljani organ za PET ispitivanje srčani mišić što će rezultirati da srce u metaboličke svrhe koristi slobodne masne kiseline pa će se videti manja akumulacija FDG u srčanom mišiću). Pacijentu treba dati instrukcije da ne jede najmanje 4-6h pre primene ^{18}F-FDG, a da bi se obezbedila hidratacija sugeriše se unos do 1l vode per os. Neposredno pre akvizicije pacijenti se savetuju da isprazne mokraćnu bešiku da bi se ograničila doza zračenja na urinarni sistem i da bi "očistili" region karlice na PET skeniranju. Kod dijabetičara koji su na terapiji insulinom, skeniranje može biti zakazano 3-4 sata nakon doručka. Doza se izračunava na osnovu telesne težine (najčešće je u rasponu od 2.5-5.5 MBk/kg ^{18}F-FDG-a). Nakon intravenske primene FDG pacijente treba utopliti (posebno mlađe) što će sprečiti i/ili smanjiti ulazak FDG-a u smeđe masno tkivo. Takođe je važno ukloniti sav metal (nakit, zubne proteze, odeću sa metalnim patentnim zatvaračima) koji bi mogli da dovedu do artefakata CT-u.

FDG PET/CT in extrapulmonary TB: Current evidence

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World Health Organization defined extrapulmonary tuberculosis as bacteriologically or clinically diagnosed tuberculosis that involves organs other than the lungs, such as pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges. Depending on which organ system is affected, tuberculosis varies in clinical symptomatology and radiological findings. Tuberculous granulomas are typically presented with an increased glucose metabolism, so areas of active tuberculosis can be differentiated from old or inactive disease. 18F-FDG PET/CT plays an important role in evaluation of extrapulmonary tuberculosis for precise identification of the activity and spread of the disease, which is crucial for further management, as well as in follow-up of therapy response. Dualtimepoint imaging is an additional technique used during routine 18F-FDG PET/CT imaging to differentiate malignancy from underlying inflammatory/infectious diseases and contributes to the reduction of false positive findings. Lymphadenitis represents around 20-40% of extrapulmonary tuberculosis, followed by pleural effusion and urogenital tuberculosis accounting for 15–20% of all cases. Any part of gastrointestinal tract can be involved, with most commonly affected distal ileum and caecum. Musculoskeletal system is involved in 1–3% of all cases. FDG PET has an outstanding potential in diagnosing tuberculous osteomyelitis, as well as arthritis typically presented as monoarthritis of large weight-bearing joints.

Keywords: Extrapulmonary Tuberculosis, 18F-FDG PET/CT, Infection, Lymphadenitis

FDG-PET u prehirurškoj evaluaciji fokalne farmakorezistentne epilepsije- Koliko nam je PET pomogao posle 160+ operacija epilepsije?

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Pozitronska emisiona tomografija (PET) pomocu 18-F-fluorodeoksiglukoze (FDG) se standardno primenjuje u neinvazivnoj fazi prehirurske evaluacije pacijenata sa fokalnom farmakorezistentnom epilepsijom. Epileptično žarište se prikazuje kao hipometabolična zona na interiktalnom PET, a kao hipermetabolična zona na iktalnom PET.

Cilj:Ukazati na značaj FDG-PET imidžinga u prehirurškoj lateralizaciji i lokalizaciji epileptičnog fokusa

Pacijenti i metode:FDG-PET/CT snimanje je obavljeno kod 471 pacijenta sa fokalnom epilepsijom (uzrasta 5-65godina). Nalazi su vizuelno analizirani (SPM analiza) i poredjeni sa epileptogenom zonom detektovanom video-EEG monitoringom i nalazom magnetne rezonance (MR)

Rezultati: Epileptično žarište je prikazano kao hipometabolična zona kod 463 pacijenta, interiktalni PET, a kod 8 pacijenata je dobijen iktalni PET- epileptogena zona je prikazana kao hipermetabolična zona. Od 160 operisanih pacijenata kod 75 (47%) je FDG-PET nalaz pomogao u identifikaciji epileptičnog žarišta. Kod svih pacijenata sa lezijom na MR, nalaz PET je bio pozitivan i saglasan sa MR nalazom, a manja hipometabolična zona na FDG-PET je sugerisala bolju prognozu operacije. Kod pacijenata sa suspektnom bilateralnom hipokampalnom sklerozom ili nesaglasnim EEG i MR nalazom PET nalaz je pomogao u lateralizaciji žarista. Kod nekih pacijenata sa inicijalno MR nelezionom epilepsijom, PET nalaz (hipometabolična zona) je ukazao na mogucu lokalizaciju fokusa sto je kasnije detaljnijom analizom MR nalaza i dopunom nalaza dodatnim sekvencama MR i koregistracijom sa PET potvrdjeno i pacijenti uspesno operisani. U slučaju neokortikalne temporalne epilepsije PET nalaz je doprineo odluci da se kod pacijenata radi leziektomija (ukoliko je postojala očuvanost metabolizma meziotemporalnih struktura) ili ako je postojao hipometabolizam da se radi temporalna lobektomija sa amigdalohipokampektomijom. FDG-PET je vizualizovao epileptično žarište kod 92,81% pacijenata.

Zaključak: FDG-PET ima značajan doprinos u lateralizaciji i lokalizacij epileptičnog fokusa u prehirurskoj evaluaciji pacijenata, posebno kod pacijenata sa normalnimnelezionim MR i ukoliko su MR i video-EEG nalaz diskordantni.Takodje veličina hipometabolične zone može pomoći u odluci o ekstenzivnosti operativnog zahvata.

The role of PET/CT imaging in the prediction of the subtype of Hodgkin lymphoma

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PET/CT together with the ex-vivo clinically relevant data, such as biopsy play an important role in the Hodgkin lymphoma (HL) patient management. Until today, the importance of the PET and CT modalities in the HL subtype prediction in unknown. This study included clinical data with multi-modal in vivo features in order to predict the subtype for HL. 88 18F-FDG PET/CT cases with patient (age, sex, weight, height and BMI) and clinical (bone marrow, spleen and lung involvement, stadium according to Lugano classification, systemic symptoms, chemo and/or radio-therapy, number of cycles and protocol employed as well as Deauville score) features were included in this study. The delineation of lymphomas on PET/CT was PET-driven (Hermes Nuclear Diagnostics, Sweden) followed by optimized radiomics feature extraction. HL subtype machine learning-driven predictive model was established . Monte Carlo cross-validation with 80% training and 20% validation sets in 1000 cross-validation folds was performed to estimate the sensitivity (SENS), specificity (SPEC), accuracy (ACC), positive-predictive-value (PPV) and negative-predictive-value (NPV) of the HL subtype predictive model. Furthermore, clinically relevant data and modality-specific averaged feature weights provided by the HL subtype predictive model were compared to identify relative importance in the prediction of subtype of HL.
Considering the fact that this is ongoing research, the results will be presented during the symposium

FDG PET/CT u dijagnostici limfoma

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Iako danas postoji stotinu radiofarmaka za PET/CT dijagnostiku onkoloških bolesti, još uvek se najčešće koristi ^{18}FDG. Osnova za primenu obeleženog analoga glukoze (deoksiglukoze) se zasniva na povišenoj aktivnosti transportera glukoze u malignoj ćeliji, tako da više glukoze ulazi u ćeliju. Metabolizam ide samo do glukozo-6 fosfata (povišena je aktivnost heksokinaza), pa glukoza ostaje zarobljena u malignoj ćeliji. Stoga se na dobijenim snimcima lako uočavaju zone povišene akumulacije ^{18}FDG na mestima gde je prisutno maligno tkivo. Kako je ^{18}FDG specifična za povišen metabolizam glukoze, a ne za malignitet, povišeno vezivanje se zapaža i u infekcijama i inflamacijama. Stoga je neophodno da nakon terapije (faktori rasta, hemio- ili radio-terapija) prođe određen vremenski period, kako bi se mogla izvršiti pouzdana kontrola.

Svi Hodgkin limfomi, svi agresivni NHL: DLBCL, mantle cell, Burkitt-ov, anaplastični, periferni Tćelijski limfom (PTCL) i najfrekventniji indolentni (sporo rastući) folikularni NHL odlično vezuju ^{18}FDG. Za sve njih je bazalni ^{18}FDG (bPET/CT) metod izbora za inicijalni stejdžing, za procenu zahvaćenosti kostne srži limfomom u HL i DLBCL NHL, procenu remisije (PET/CT je standardna procedura), procenu odgovora na terapiju.

Procena odgovora na terapiju (PET Response Evaluation Criteria In Solid Tumors, PRECIST), se vrši stepenovanjem akumulacije ^{18}FDG u tkivu limfoma (Deauville skala od 5 poena): 1) nema akumulacije; 2) akumulacija je jednaka ili niža od medijastinalne; 3) viša je od medijastinalne, a niža ili jednaka onoj u tkivu jetre; 4) viša je od one u jetri; 5) 2-3 puta je viša od one u jetri i/ili nove lezije. U bolesnika koji ne reaguju dobro na terapiju, razmišlja se o eskalaciji terapije. Kako ne bi došlo do predoziranja bolesnika, normalan PET/CT podrazumeva Deauville skor 1, 2 i 3, a patološki Deauville skor 4 i 5. U slučajevima kada se razmišlja o smanjenju terapije (de-eskalaciji), normalan PET/CT podrazumeva Deauville skor 1 i 2, a patološki Deauville skor 3, 4, i 5, kako ne bi došlo do subdoziranja bolesnika. Ranije je procena odgovora na terapiju vršena na kraju terapije (ePET/CT). Velika ušteda i bolja efikasnost terapije se dobija ranom procenom odgovora na terapiju (već posle 2-3 ciklusa hemioterapije): interim PET (iPET/CT).

Korak dalje je učinjen **Lugano klasifikacijom**. Kategorije metaboličkog odgovora su određene na osnovu Deauville skor-a. Kompletan metabolički odgovor (**CMR**) podrazumeva Deauville skor 1, 2, i 3 pri standardnoj terapiji, a Deauville skor 1 i 2 pri de-eskalaciji terapije. Parcijalni metabolički odgovor (**PMR**) podrazumeva Deauville score 4 i 5, sa smanjenom akumulacijom ^{18}FDG u poređenju sa preterapijskom i sa rezidualnom masom bilo koje veličine. Na interim PET-u PMR znači da bolest reaguje na terapiju, a na kraju terapije ukazuje na rezidualnu bolest. Bez metaboličkog odgovora (**NMR**) podrazumeva Deauville score 4 i 5, bez značajne promene akumulacije ^{18}FDG u poređenju sa preterapijskom kako na interim PET-u, tako i na kraju terapije. Progresivna metabolička bolest (**PMD**) podrazumeva Deauville score 4 i 5 sa povećanom akumulacijom ^{18}FDG u poređenju sa preterapijskim PET-om, i/ili nove fokuse akumulcije ^{18}FDG povezani sa limfomom, bilo na interim PET-u ili na kraju terapije.

Lugano klasifikacija je postala standard u stejdžingu, kao i u proceni odgovora na terapiju (na iPETu i na ePET-u) u bolesnika sa limfomom. Preporučuje se rutinska upotreba of ^{18}FDG-PET/CT kao zlatnog standarda za stejdžing FDG-avidnih limfoma: HL, DLBCL NHL, folikularnog NHL i mantle

cell NHL. Lugano klasifikacija je eliminisala upotrebu biopsije kosti u HL i u većini DLBCL. Novi kvantitativni PET metodi za procenu odgovora na terapiju (qPET) su metabolički volumen tumora (**MTV**, koji predstavlja zbir svih volumena tumorskog kiva na PET/CT-u) i totalna glikoliza u leziji (**TLG,** TLG = SUVmeanTU x MTV). Oba su pouzdani pokazatelji vijabilne tumorske mase, bolji od ranije korišćenog „bulk"-a na CT-u.

Rezidualne mase na kraju terapije limfoma su česte: javljaju se u 70 % HL i 50 % NHL. Međutim, mali procenat tih bolesnika zbilja ima recidiv: manje od 20 % HL i 25 % NHL. Ukoliko u rezidualnoj masi nema nakupljanja ^{18}FDG radi se o kompletnoj metaboličkoj remisiji. Ukoliko je prisutno nakupljanje, potrebna je biopsija ili kontrolni PET/CT (da li se metabolička aktivnost smanjuje?).

Za bolesnika sa retkim indolentnim non-Hodgkin limfomoma koji inicijalno ne nakupljaju ^{18}FDG (marginal zone, MALT, B-CLL/SLL, limfoplazmocitni limfom, primarni kožni T ćelijski limfom), i dalje važi ranije postojeće pravilo da se inicijalno snimanje i procena odgovora na terapiju vrši CT-om.

Pitfalls in PET/CT diagnosis of TBC

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Tuberculosis is known to be a great mimicker as it can masquerade as various number of inflammatory or malignant disorders. One of the main drawbacks of FDG PET/CT is its lack of specificity in order to distinguish between different inflammations and/or malignancies. Patients with cancer are more prone to develop active tuberculosis, and vice versa, TB patients are in greater risk of lung cancer comparing to normal population. Dual-phase FDG PET imaging has been tried in the differentiation of inflammation from malignancy with some promising results, but there are some controversies when it comes to patients with tuberculosis. On the other hand, there are some inflammatory diseases such as sarcoidosis, also infections with other Mycobacterium species, which could be mistaken for TB on FDG PET/CT. Some difficulties in evaluation of disease activity and therapy response on FDG PET/CT have also been reported even in individuals with confirmed diagnosis of TB. Altogether, tuberculosis on FDG PET/CT can have a myriad of manifestation that sometimes can be perplexing to interpret even for experienced reader.

Positron emission tomography in neurooncology, selected topics

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Abstract

Defining glioma borders against healthy brain tissue is among the most important tusks in preoperative neurooncologic diagnostics, bearing in mind that gliomas, even in their earliest development, infiltrate brain far beyond borders depicted radiologically as well as those observable during surgery. Since standard, anatomic, radiology diagnostics is, in this regard, less than satisfying, usefulness of functional visualization methods is under research, notably advanced magnetic resonance (MR) techniques and positron emission tomography (PET) procedures. A high molecular sensitivity, together with application of various molecular probes labeled with positron emitters, give PET an advantage regarding the non-invasive tissue characterization, which is the key to the differentiation of peritumoral healthy brain tissue from apparently normal but infiltrated brain tissue, being the source of postoperative glioma recurrence.

The most important indication for PET in the post therapy follow-up is the differentiation of adverse effects of radio and chemo therapy from glioma recurrence, in which indication the standard radiologic diagnostics is unreliable, too. In addition to cerebral radiation necrosis, the well-known complication of postsurgical radiation therapy for brain tumors, researchers in recent literature use novel terms like pseudo-progression and pseudo-response to describe various confounding conditions associated with newly introduced therapies.

Recent advances in automated quantitative processing of imaging studies (radiomics and radiogenomics) are credited with a potential to improve personalized treatment of brain tumors. PET should have an important role in these new approaches.

In present work some of the most relevant results of recent research regarding possible role of PET procedures in neurooncologic indications are pointed out and expert recommendations are presented.

Key words: brain tumor, positron emission tomography, chemoradiotherapy, pseudoprogression, radiation necrosis, radiogenomics.

Inflamacije i infekcije u plućima-radiološka dilema

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Neinfektivne upalne plućne bolesti su klinički, radiološki i histopatološki heterogena grupa akutnih i hroničnih stanja. Ovi poremećaji mogu zahvatiti vazdušne prostore, plućne krvne sudove, intersticijum, ili kombinaciju ova tri anatomska dela. Neinfektivne inflamatorne bolesti pluća mogu biti idiopatske ili predstavljati sekundarnu reakciju na autoimune bolesti, infekciju, izlaganje okolini ili lekove. Predstavnici oboljenja parenhima su eozinofilna i organizujuća pneumonija, histiocitoza, RB-ILD i hipersenizitivni pneumonitis. Vaskularne bolesti obuhvataju non ANCA i ANCA vaskulitise, lekovima indukovane vaskulitise i promene u okviru sistemskig kolagenih bolesti. U intersticijumska oboljenja spadaju idiopatske intersticijumske pneumonije, sarkoidoza i profesionalna oboljenja. Radiološke metode igraju ključnu ulogu u otkrivanju i karakterizaciji neinfektivnih upalnih plućnih bolesti. Radiološke manifestacije ovih oboljenja su često nespecifične i uključuju nodularne promene, konsolidacije, difuzne mikronoduse i zadebljanja intersticijuma. Infekcije u plućima se mogu manifestovati širokim spektrom promena. Značaj imaging metoda je u prikazu opsežnosti same promene, eventualnog uzroka i pratećih komplikacija infekcije. Iako CT nije inicijalna metoda u dijagnostici ovih stanja, znatno je senzitivnija i specifičnija od radiografije. Na osnovu opsežnosti i distribucije, moguće je izdiferencirati bakterijske bronhopneumonije od gljivičnih i idiopastkih hroničnih pneumonija. Neretko uzrok pneumonije mogu biti endobronhijalni tumori što se na radiografiji ne vidi. Tuberkuloza, virusne pneumonije i mikoze se često manifestuju mikronodularnim promenam i njihovo međusobno razlikovanje i diferenciranje od neinfektivnih obolenja je vrlo važno.

Zaključak: inflamatorne i infektivne plućne bolesti imaju različite radiološke manifestacije koje su važne za ispravnu dijagnozu. Zbog toga, radiolozi moraju razumeti njihove kliničke manifestacije i patološke uzroke da bi uz odgovarajući radiološki nalaz sugerisali odgovarajuću dijagnozu.

Dual tracer imaging; 18F- bone scanning and PSMA imaging in selection of CRPC patients for targeted radionuclide bone treatments

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Two different molecular radio-theragnostic principles are applied in prostate cancer. Firstly, radiopharmaceuticals with the same or similar mechanism of action but different energy

(positron-β+, e.g. ^{18}F- sodium fluoride [NaF] or gamma-γ, eg ^{99m}Tc-diphosphonates emitting isotopes) can be used to identify patients with osteoblastic metastases for a treatment with bone seeking beta (β-) or alpha (α) emitting radionuclides to deliver targeted molecular radiotherapy. An alpha emitting ^{223}Ra-dichloride is a first proof of principle for targeted alpha particle treatment in the clinical setting, which has demonstrated significantly improved overall survival in patients with castration-resistant prostate cancer (CRPC) and predominant bone metastases. The second principle involves utilisation of the same prostatic specific membrane antigen (PSMA) or similar compound (eg PSMA-11, PSMA-617), but different label with

either β+ (^{68}Ga or ^{18}F) or γ (^{99m}Tc) emitting radioisotope for imaging and subsequently β- (^{177}Lu) or α (^{225}Ac) emitting radionuclide for treatment.

The diagnostic performance of ^{68}Ga PSMA or ^{18}F PSMA PET/CT in the evaluation of bone metastases in patients with CRPC selected for radionuclide therapy in comparison to ^{18}F-NaF PET-CT has not been fully established. Combined dual tracer PET imaging (e.g. ^{68}Ga-PSMA or ^{18}F-PSMA and ^{18}F-NaF) may need to be utilised for selection of patients with CRPC and skeletal metastases prior to initiation or modification of targeted radionuclide bone therapy and also possibly for treatment response. Combination of PSMA therapy with existing therapy modalities such as ^{223}Ra-chloride or antiandrogen therapy should also be investigated in prospective clinical multicentre trials to provide a personalised management for those patients.

PET/CT in diagnosis of colorectal carcinomas

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Colorectal carcinoma (CRC) represents the third most common malignant tumor in both men and women in developed world and the second leading cause of cancer-related death. Despite the advances in surgical treatment and introduction of combined therapeutical modalities, 5 years survival rarely exceeds 60%, varying from 90% in localized disease to 11% in patients with spread to distant organs. Between 55% and 80% of patients will develop recurrence, with isolated hepatic recurrence initially occurring in approximately 30% of patients. Overall, liver metastases represent leading cause of cancer-related morbidity and mortality in colorectal cancer.

At present, whole-body fluorine-18-fluoro-deoxyglucose positron emission tomography/computed tomography (FDG PET/CT) represents an advanced diagnostic imaging technique in detecting loco-regional recurrence and metastases in postoperative patients with colorectal carcinoma owing to its high sensitivity and accuracy. Current guidelines for managing patients with CRC after therapy recommend regular measurements of serum carcinoembryogenic antigen (CEA) and imaging tests. CEA, although sensitive in detecting early relapse, gives very often a false-positive result.

The established role of FDG PET/CT in diagnosis of colorectal cancer includes differentiation between fibrosis and scar tissue from viable tumor in residual masses of rectal cancer, localization of recurrence in patients with an unexplained rise in serum carcinoembryonic antigen (CEA) and staging before surgical resection of recurrent disease. In addition, FDG PET/CT has role in prediction and assessment of therapy response in CRC patients, especially in cases of locally advanced rectal cancer, as well as in response evaluation after local ablative therapy of liver metastases and chemotherapy in advanced colorectal cancer. The biological effects of therapy, shown on PET/CT studies, are thought to be of stronger prognostic significance compared to anatomical changes. However, the role of FDG PET/CT in initial staging of colorectal cancer is not fully established and is not routinely recommended by current guidelines. One of the emerging roles of FDG PET/CT in the setting of locally advanced rectal cancer is determination of target volume for radiotherapy planning.

The usefulness of FDG PET/CT in colorectal cancer patients has also been confirmed through identification of high-risk groups of patients for disease recurrence and progression, in order to optimize and individualize treatment in specific cases and improve progressionfree and overall survival.

PET/CT IN DIAGNOSIS OF HEPATOBILIARY TUMORS

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The utility of PET/CT in imaging diseases of hepatobiliary system varies according to the type, location of the lesion, radiopharmaceutical applied as well as according to indication.

Sensitivity in the detection of intrahepatic **HCC**, is limited (50-70%). However, since poorlydifferentiated HCC show high FDG uptake, the degree of differentiation can be predicted, as well as prognosis. Further, poorly differentiated HCC is frequently associated with metastasis and recurrence, which can be detected by FDG/PET. However, if metastases of HCC are suspected, FDG has better diagnostic performance, in particular in sites where CT has suboptimal sensitivity, such as bone metastases or non-enlarged lymph nodes. FDG can be used for selecting HCC patients eligible for liver transplantation and to predict recurrence. FDG is also able to detect HCC recurrence of FDG avid HCC. The combined use of FDG and lipid tracer is best way to detect HCC metastases.

Cholangiocarcinoma is frequently highly FDG avid and can be visualised if sufficient tumour volume is present. However, hilar and extrahepatic cholangiocarcinoma usually show lower activity than peripheral cholangiocarcinoma. In cholangiocarcinoma, except for infiltrating type, PET/CT is useful for detection of recurrent and metastatic disease and for assessment of treatment response.

For the detection of **primary gallbladder carcinoma**, FDG-PET has a sensitivity of 75-100% and specificity of 80-89%. However, US, MRI, and contrast-enhanced CT are better for the detection of this cancer. The primary role of FDG PET is to identify distant metastases and recurrence.

Other PET radiopharmaceuticals can also be used.

PET in musculoskeletal imaging

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In the last few decades, with the introduction in clinical practice of different novel radiotracers, PET/CT gained a major role in orthopedics imaging, also in oncological field. The integration of anatomical data deriving from low dose CT images, fundamental for bone imaging, and of functional information obtained from the variety of new radiotracers, gives the opportunity to the nuclear medicine physician to have a complete information about different characteristics of the tumor lesion or to better define various clinical scenarios of the benign diseases. In this short presentation I will give an overlook of the major indications for PET/CT imaging in orthopedics.