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Original

Detection of a second primary cancer in a ^{18}F-fluorocholine PET/CT – multicentre retrospective analysis on a group of 1345 prostate cancer patients

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Abstract

Background: Aim of this study was to evaluate the rate of incidental detection of second primary cancer (SPC) at ^{18}F-fluorocholine ([^{18}F]FCH) positron emission tomography/computed tomography (PET/CT) performed in prostate cancer patients.

Material and methods: A retrospective analysis was performed on a group of 1345 prostate cancer patients, who underwent [^{18}F]FCH PET/CT study because of suspicion of recurrence (n = 937) or for initial staging (n = 408). Images were acquired after intravenous injection [^{18}F]FCH with a mean activity of 200 ± 75 MBq (5.4 ± 2 mCi), from the top of the head to the half of the thigh. The confirmation of second primary cancer was obtained from the cancer registry.

Results: Based on the [^{18}F]FCH PET/CT scans, a second primary cancer was suspected in 89 patients (6.6%). Of these, a malignancy was histologically confirmed in 26 patients (29% of all suspected findings and 1.9% of the complete cohort). Lung cancer (including adenocarcinoma, neuroendocrine cancer) was diagnosed in 13 patients (50%) and hematologic neoplasm (including chronic lymphocytic leukemia, Hodgkin lymphoma, follicular lymphoma, and multiple myeloma) in 5 patients (19%). ^{18}F-fluorocholine PET/CT also revealed esophageal cancer, mesothelioma, testicular, renal, bladder, and colorectal cancer in individual patients, non-keratinizing squamous cell carcinoma (SCC) of the skin as well as head and neck SCC with unknown primary.

Conclusion: We conclude that incidental detection of a second primary cancer in prostate cancer patients using [^{18}F]FCH PET/CT is not very common and that lung cancer and hematologic malignancies are most frequently detected.

KEY words: positron emission tomography/computed tomography; prostate cancer; second primary cancer

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Introduction

Prostate cancer (PCa) ranks 2nd in incidence and 5th in mortality in men worldwide, accounting for 1.3 million newly diagnosed cases and 359.00 deaths per annum [1]. The term 'second primary cancer' (SPC) is used to describe a malignancy that appears unrelated to treated or untreated primary malignancy and that might occur months or years after primary diagnosis. In general, SPC is seen in ca. 15% of cancer patients, leading to increased morbidity and mortality. When suspicion of an SPC is raised, the metastasis of the first primary malignancy should be excluded at first [2, 3].

Standard positron emission tomography/computed tomography (PET/CT) examination with ^{18}F-Fluorodeoxyglucose ([^{18}F]FDG) has a limited value in the diagnosis of prostate cancer and, for this reason, some other radiopharmaceuticals, including tracers based on the metabolism of choline are used, e.g. ^{11}C-choline or ^{18}F-fluorocholine [4–6]. Radiolabelled choline accumulation in prostate cancer can be observed because of its integration into membranes of the proliferating tumor cells [7]. PET/CT with the radiolabeled choline plays an important role in the initial staging, evaluation of recurrence, and dissemination of prostate cancer [8–11]. The detection of SPC is clinically relevant since comorbidities, including concomitant malignancies, may pose a clinical problem in men with prostate cancer.

The aim of this study was to evaluate the rate of incidental detection of a second primary cancer at [^{18}F]FCH PET/CT in patients with prostate cancer.

Material and methods

The retrospective, multicenter analysis was performed in 1345 prostate cancer patients, who underwent standard [^{18}F]FCH PET/CT examination in three nuclear medicine departments between May 2009 and October 2019 because of the suspicion of recurrence (n = 937) or for the initial staging (n = 408). The images were acquired from skull vertex to mid-thigh 45–60 min after IV injection of 200 ± 75 MBq (5.4 ± 2 mCi) of [^{18}F]FCH. All patients fasted for 6 h before examination and they gave their written informed consent. The images were acquired with different scanners depending on the study site: Gemini TF 16 (Philips), Discovery ST or Discovery IQ (GE Healthcare), Biograph mCT S(64)-4R (Siemens). All PET/CT images were fused and viewed using a dedicated workstation in sagittal, coronal, and transverse planes.

The inclusion criteria for SPC included unspecific [^{18}F]FCH uptake, not related to patients' previous clinical history. From the selected group of suspected SPC, [^{18}F]FCH PET images, as well as reports, were re-reviewed for the independent nuclear medicine specialists, and the confirmation of SPC was obtained from the histopathological examination of the suspected lesions. The final SPC diagnosis was retrieved from the local and national cancer registries and was defined using the Warren and Gates' criteria [12].

Results

Based on the [^{18}F]FCH PET/CT scans, an SPC was suspected in 89 patients (6.6%) from the whole analyzed group. Of these, a malignancy was confirmed in 26 patients (29.2% of all suspected findings and 1.9% of the complete cohort). Most of the patients were referred to [^{18}F]FCH PET/CT examination for suspicion of recurrence (n = 21 patients) and only 5 of them for initial staging. The characteristics of patients with confirmed SPC are shown in Table 1.

The most common SPC was lung cancer (including adenocarcinoma, neuroendocrine cancer), which was diagnosed in 13 patients (50%), and hematologic malignancy (including chronic lymphocytic leukemia, Hodgkin lymphoma, follicular lymphoma, and multiple myeloma diagnosed in 5 patients (19.2%) (Fig. 1). ^{18}F-fluorocholine PET/CT also revealed a low-differentiated adenocarcinoma of the esophagus, mesothelioma, a testicular seminoma (Fig. 2), renal cancer, a bladder and colorectal cancer in individual patients. Furthermore, a non-keratinizing squamous cell carcinoma (SCC) of the skin was diagnosed in one patient. In another patient, [^{18}F]FCH PET/CT showed increased uptake in cervical lymph nodes that were histologically verified as SCC metastases and the primary malignancy remained undetected (cancer of unknown primary syndrome). All patients with confirmed SPC underwent treatment first for SPC (because in most cases it was more aggressive) and only in a patient with chronic lymphocytic leukemia, first, the progression of PCa was treated.

Discussion

Second primary cancers are relatively rare, reported in a wide range of 0.4–17% of PET/CT scans [13–20]. The detection of SPC has been more frequently reported for PET/CT scans using [^{18}F]FDG than using [^{18}F]FCH. A quite high number of SPC is found in patients with head and neck cancer, lymphoma, and gynecological malignancies [13–20]. The risk of development of any SPC increases with time from initial cancer diagnosis [21]. Detection of SPC in prostate cancer patients using a tracer other than [^{18}F]FDG is very rare, with a frequency of 1.54–13%, with the specificity of 47–90% and sensitivity of 84–100% [22, 23], however, several authors found an SPC in [^{18}F]FCH PET/CT study (Tab. 2) with SUV_{max} value for SPC ranged from 2.7–15.

To our knowledge, this is the largest cohort of [^{18}F]FCH PET/CT scans reviewed retrospectively for the detection of SPC. A confirmed synchronous malignancy was detected in 1.9% of patients, but potentially malignant findings were much more frequent, accounting for as much as 6.6% of all scans, suggesting a relatively low specificity of this imaging modality.

Other authors reported an incidental uptake of [^{18}F]FCH in the head and neck of patients with prostate cancer. An incidental uptake of [^{18}F]FCH in the head and neck region was found in 8 patients examined for prostate cancer staging or restaging [27]. However, only in two cases, malignancy was proven histologically, in other cases the increased uptake was associated with a benign finding. In our study, one patient showed enlarged cervical lymph nodes with elevated uptake of [^{18}F]FCH (SUV_{max} 1.8) and after further work-up, the SCC with unknown primary malignancy was diagnosed. Calabria et al. reported [^{18}F]FCH-positive findings unrelated to PCa in 48 out of 300 patients (16%), but only a few of them were finally confirmed as malignant diseases (colorectal cancer, multiple myeloma, and bladder cancer) [28].

Pieterman et al. compared ^{11}C-choline and [^{18}F]FDG in the diagnosis of primary lung cancer and reported no significant differences between these two tracers, however, [^{18}F]FDG was more accurate in the detection of nodal involvement than ^{11}C-choline [29].

Table 1. Characteristics of patients with a second primary cancer detected in ^{18}F-fluorocholine

N⁰	Age	Indication to [18F]FCH PET/CT	PSA (ng/mL)	Second primary cancer	SUV_{max} of the second primary cancer
1	56	PCa recurrence	0.426	Lung adenocarcinoma	2.3
2	75	PCa recurrence	4.23	Lung adenocarcinoma	8.2
3	61	PCa recurrence	6.37	Lung adenocarcinoma	2.5
4	63	PCa recurrence	0.54	Neuroendocrine lung cancer	2.4
5	80	PCa staging	n/a	Lung adenocarcinoma	4.6
6	65	PCa staging	10.4	Chronic lymphocytic leukemia	3.8
7	56	PCa recurrence	0.01	Hodgkin lymphoma	4.7
8	75	PCa recurrence	2.6	Testicular seminoma	5.3
9	72	PCa recurrence	0.003	Colorectal cancer	5.7
10	63	PCa recurrence	3.76	Solid lung cancer	2.6
11	65	PCa recurrence	47.58	Adenocarcinoma of the esophagus	7.7
12	78	PCa recurrence	30.0	Multiple myeloma	3.4
13	71	PCa recurrence	11.68	Clear cell renal cancer	4.9
14	71	PCa staging	20.0	Follicular lymphoma	4.5
15	75	PCa recurrence	0.06	Lung adenocarcinoma	5.1
16	63	PCa staging	7.29	Lung adenocarcinoma	4.8
17	75	PCa recurrence	n/a	Lung adenocarcinoma	1.2
18	59	PCa staging	3.65	Lung adenocarcinoma	3.2
19	74	PCa recurrence	0.3	Mesothelioma	5.4
20	79	PCa recurrence	5.74	Bladder cancer	11.0
21	67	PCa recurrence	10.78	Lung adenocarcinoma	2.2
22	69	PCa recurrence	0.08	Non-keratinizing cutaneous SCC	4.1
23	65	PCa recurrence	9.47	Chronic lymphocytic leukemia	3.3
24	75	PCa recurrence	0.57	Lung adenocarcinoma	6.0
25	86	PCa recurrence	2.53	Lung adenocarcinoma	1.8
26	73	PCa recurrence	1.06	SCC with unknown primary malignancy	1.8

n/a — not available; PCa — prostate cancer; SCC — squamous cell carcinoma; SUVmax —maximum standardized uptake value

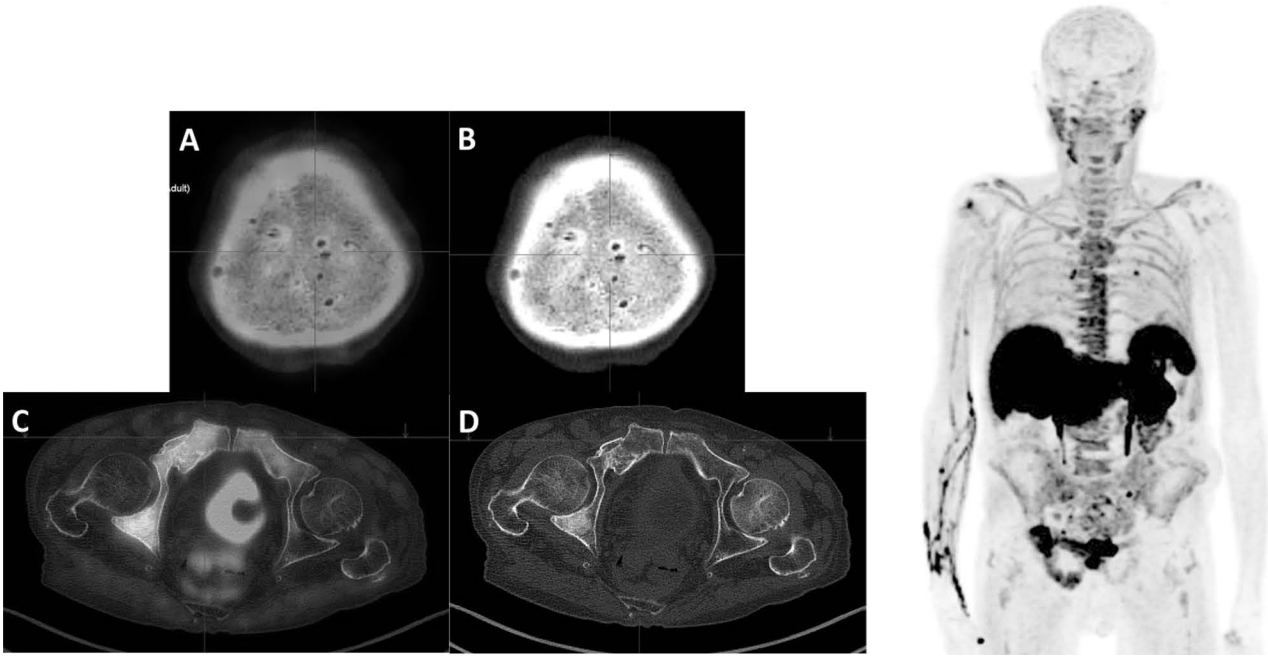

Figure 1. 78-year-old man with PCa, PSA 30.0 [ng/ml] and synchronous multiple myeloma. **A** — PET/CT fusion without increased [18F]FCH uptake in the skull but with osteolytic lesions in CT. **B** — CT showing osteolytic lesions of the multiple myeloma in the skull. **C** — PET/CT fusion image with extensive prostate metastases in the right iliac bone. **D** — CT with bone remodeling as a result of metastatic changes

Table 2. Second primary cancers detected at ^{18}F-fluorocholine positron emission tomography/computed tomography (PET/CT) in patients with biochemical prostate cancer recurrence — overview of the literature

Author	PCa treatment (s)	Age	PSA (ng/mL)	Second primary cancer histology	Second primary cancer treatment
Sollini M. et al. [24]	RP (2004) + ADT	72	0.11	NSCLC — Adenocarcinoma	CHT + palliative EBRT
	RP (1998) + salvage EBRT (2009)	71	0.08	NSCLC — n/a	CHT
	EBRT (1996)	80	2.62	NSCLC — n/a	patient refused any treatment
	RP (2003)	80	8.77	Melanoma — Melanoma metastases	excision of melanoma metastases
	EBRT (2003) + ADT	71	3.16	NSCLC — n/a	lung lobectomy + salvage EBRT
	RP (2012)	74	1.4	NSCLC — n/a	lung lobectomy + salvage EBRT
	RP (2012) + ADT	80	0.3	Colorectal cancer — n/a	anterior resection of rectum + ADT
Buroni F. et al. [25]	BRT	71	2.86	DLBCL	CHT
Tuscano et al. [26]	n/a	66	5.2	posterior wall of sigmoid colon — mucinous adenocarcinoma	surgical resection

RP — radical prostatectomy; BRT — brachytherapy; ADT — androgen deprivation therapy; EBRT — external beam radiation therapy; DLBCL — Diffuse Large B Cell Lymphoma; CHT — chemotherapy; NSCLC — non-small-cell lung cancer; n/a — not available

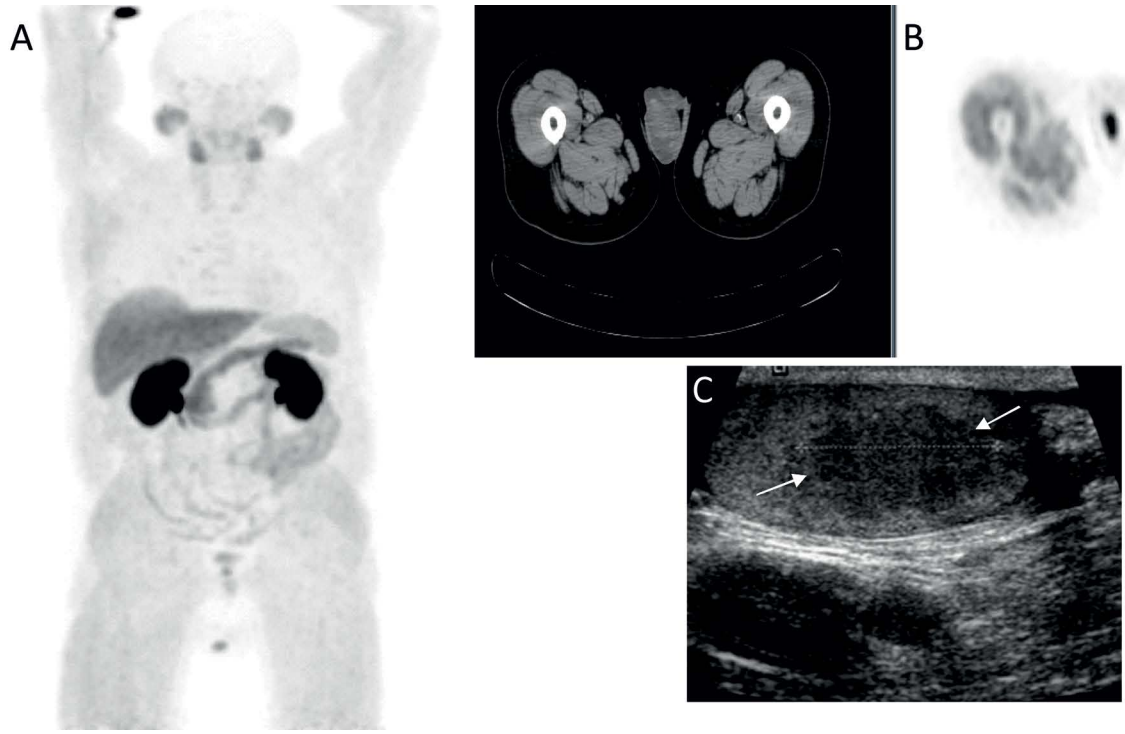

Figure 2. 75-year-old man with PCa, T-PSA 2.6 [ng/ml] and synchronous testicular seminoma. **A** — MIP image without typical metastatic changes of PCa. **B** — increased [18F]FCH uptake in the right testicle. **C** — hypoechogenic mass with increased vascularity in the ultrasound, typical for seminoma

It is well-known that [^{18}F]FCH PET/CT shows optimal diagnostic accuracy when used in patients with relatively high concentrations of prostate-specific antigen (PSA), at least above 1.0 ng/mL [30]. As shown in Table 1, there were several patients who were reported to PET/CT despite PSA levels below that cut-off value. The retrospective analysis of these cases showed that clinical deterioration rather than PSA concentration was a major indication to PET/CT. The clinical symptoms, like loss of weight or dyspnea, had driven the diagnostic process to the exclusion of PCa progression before initiating further symptom-oriented diagnosis. In general, patients with low PSA concentrations would benefit more from [^{68}Ga]Ga-PSMA PET/CT — a radiopharmaceutical known for its higher sensitivity in the detection of PCa relapse in the presence of lower cancer burden [30], however, due to better local availability [^{18}F]FCH PET/CT was applied instead. Although, as expected, the scan was negative with respect to the PCa in all cases with PSA < 1.0 ng/mL, the patients benefited from the earlier detection of the second primary malignancies, so that an adequate treatment could be initiated immediately.

Our retrospective study has several drawbacks. The study group was not homogenous from the technical point of view, since images were obtained using four different PET/CT scanners in three centers over a long period of 10 years. Although all the scanners were equipped with 16-slice CT and the imaging parameters were similar, the impact of differences in qualitative parameters on the diagnostic accuracy cannot be excluded. On the

other hand, it would not be possible to collect such a large study cohort on the basis of experience gathered in one center only or a shorter interval. Our analysis was limited to the histopathologically confirmed malignancies, reported to the cancer registers. Positively verified lesions accounted for 29% of all suspected lesions, but we have to keep in mind that this number might be underestimated. It cannot be excluded that some cases were lost to analysis if the findings reported in [18F]FCH PET/CT were not subjected to further verification due to the patient's refusal or poor clinical condition that led to disqualification from invasive diagnostic procedures. Conversely, we did not analyze benign findings (false-positive results), so that adequate statistical analysis of the diagnostic accuracy of this method could not be performed and this will be considered in our next paper.

Conclusions

The study showed that incidental detection of a second primary cancer in prostate cancer patients using [18F]FCH PET/CT is not very common and that lung cancer and hematologic malignancies belong to the most frequent cancers detected. Therefore, each unusual radiotracer uptake that is unlikely to be related to prostate cancer should be verified with other methods, including histopathology.

Conflict of interest

The authors declare no conflict of interest.

References

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018; 68(6): 394–424, doi: 10.3322/caac.21492, indexed in Pubmed: 30207593.
2. Feller L, Lemmer J. New 'second primary' cancers. SADJ. 2012; 67(4): 175–178, indexed in Pubmed: 23198353.
3. Nielsen SF, Nordestgaard BG, Bojesen SE. Associations between first and second primary cancers: a population-based study. CMAJ. 2012; 184(1): E57–E69, doi: 10.1503/cmaj.110167, indexed in Pubmed: 22125331.
4. Vali R, Loidl W, Pirich C, et al. Imaging of prostate cancer with PET/CT using (18)F-Fluorocholine. Am J Nucl Med Mol Imaging. 2015; 5(2): 96–108, indexed in Pubmed: 25973332.
5. Kwee SA, DeGrado TR, Talbot JN, et al. Cancer imaging with fluorine-18-labeled choline derivatives. Semin Nucl Med. 2007; 37(6): 420–428, doi: 10.1053/j.semnuclmed.2007.07.003, indexed in Pubmed: 17920349.
6. Beheshti M, Haroon A, Bomanji JB, et al. Fluorocholine PET/computed tomography: physiologic uptake, benign findings, and pitfalls. PET Clin. 2014; 9(3): 299–306, doi: 10.1016/j.cpet.2014.03.001, indexed in Pubmed: 25030393.
7. Yoshimoto M, Waki A, Yonekura Y, et al. Characterization of acetate metabolism in tumor cells in relation to cell proliferation: acetate metabolism in tumor cells. Nucl Med Biol. 2001; 28(2): 117–122, doi: 10.1016/s0969-8051(00)00195-5, indexed in Pubmed: 11295421.
8. Evangelista L, Cimitan M, Zattoni F, et al. Comparison between conventional imaging (abdominal-pelvic computed tomography and bone scan) and [(18)F]choline positron emission tomography/computed tomography imaging for the initial staging of patients with intermediate- tohigh-risk prostate cancer: A retrospective analysis. Scand J Urol. 2015; 49(5): 345–353, doi: 10.3109/21681805.2015.1005665, indexed in Pubmed: 25649494.
9. Fanti S, Minozzi S, Castellucci P, et al. PET/CT with (11)C-choline for evaluation of prostate cancer patients with biochemical recurrence: meta-analysis and critical review of available data. Eur J Nucl Med Mol Imaging. 2016; 43(1): 55–69, doi: 10.1007/s00259-015-3202-7, indexed in Pubmed: 26450693.
10. Picchio M, Messa C, Landoni C, et al. Value of [11C]choline-positron emission tomography for re-staging prostate cancer: a comparison with [18F]fluorodeoxyglucose-positron emission tomography. J Urol. 2003; 169(4): 1337–1340, doi: 10.1097/01.ju.0000056901.95996.43, indexed in Pubmed: 12629355.
11. Gauvin S, Rompré-Brodeur A, Chaussé G, et al. F-fluorocholine positron emission tomography-computed tomography (F-FCH PET/CT) for staging of high-risk prostate cancer patients. Can Urol Assoc J. 2019; 13(4): 84–91, doi: 10.5489/cuaj.5142, indexed in Pubmed: 30273114.
12. Warren S, Gates O. Multiple primary malignant tumors: A survey of the literature and statistical study. Am J Cancer. 1932; 16: 1358–1414.
13. Chun-Sing W, Nan-Jie G, Yiu-Ching C. Prevalence of synchronous second primary malignancy: identification using whole body PET/CT imaging. Clin Imaging. 2014; 38(2): 179–186, doi: 10.1016/j.clinimag.2013.09.001, indexed in Pubmed: 24210360.
14. Garcheva M, Zlatareva D, Gocheva L. Positron emission tomography combined with computed tomography for diagnosis of synchronous tumors. Klin Onkol. 2014; 27(4): 283–286, doi: 10.14735/amko2014283, indexed in Pubmed: 25115718.
15. Moletta L, Bissoli S, Fantin A, et al. PET/CT incidental detection of second tumor in patients investigated for pancreatic neoplasms. BMC Cancer. 2018; 18(1): 531, doi: 10.1186/s12885-018-4469-4, indexed in Pubmed: 29728085.
16. Pang L, Liu G, Shi H, et al. Nineteen cases with synchronous multiple primary cancers studied by 18 F-FDG PET/CT. Hell J Nucl Med. 2017; 20(1): 36–40, doi: 10.1967/s002449910504, indexed in Pubmed: 28315906.
17. Gunes BY, Akbayır O, Demirci E, et al. Clinical, pathological and (18)F-FDG PET/CT findings in synchronous primary vaginal and endometrial cancers. Hell J Nucl Med. 2016; 19(2): 170–172, doi: 10.1967/s002449910374, indexed in Pubmed: 27331214.
18. Płachta M, Cholewiński W, Burchardt E, et al. Strategy and early results of treatment of advanced cervical cancer patients with synchronous cancers observed in PET-CT imaging. Ginekol Pol. 2017; 88(9): 475–480, doi: 10.5603/GP.a2017.0087, indexed in Pubmed: 29057432.
19. Strobel K, Haerle SK, Stoeckli SJ, et al. Head and neck squamous cell carcinoma (HNSCC)--detection of synchronous primaries with (18) F-FDG-PET/CT. Eur J Nucl Med Mol Imaging. 2009; 36(6): 919–927, doi: 10.1007/s00259-009-1064-6, indexed in Pubmed: 19205699.
20. Miyazaki T, Sohda M, Higuchi T, et al. Effectiveness of FDG-PET in screening of synchronous cancer of other organs in patients with esophageal cancer. Anticancer Res. 2014; 34(1): 283–287, indexed in Pubmed: 24403475.
21. Amer MH. Multiple neoplasms, single primaries, and patient survival. Cancer Manag Res. 2014; 6: 119–134, doi: 10.2147/CMAR.S57378, indexed in Pubmed: 24623992.
22. How Kit N, Dugué AE, Sevin E, et al. Pairwise comparison of 18F-FDG and 18F-FCH PET/CT in prostate cancer patients with rising PSA and known or suspected second malignancy. Nucl Med Commun. 2016; 37(4): 348–355, doi: 10.1097/MNM.0000000000000457, indexed in Pubmed: 26642435.
23. García JR, Ponce A, Canales M, et al. [Detection of second tumors in 11C-choline PET/CT studies performed due to biochemical recurrence of prostate cancer]. Rev Esp Med Nucl Imagen Mol. 2014; 33(1): 28–31, doi: 10.1016/j.remn.2013.01.007, indexed in Pubmed: 23499124.
24. Sollini M, Pasqualetti F, Perri M, et al. Detection of a second malignancy in prostate cancer patients by using [(18)F]Choline PET/CT: a case series. Cancer Imaging. 2016; 16(1): 27, doi: 10.1186/s40644-016-0085-1, indexed in Pubmed: 27581366.

25. Buroni FE, Persico MG, Lodola L, et al. Malignant Lymphoma Imaged by 18F-Fluoro-Choline PET-CT in a Patient with Prostate Cancer: a Case Report and Review of Literatureostate Cancer: A Case Report and Review of the Literature. STJ Cancer. 2017; 1(1002).
26. Tuscano C, Russi EG, Al Sayyad S, et al. An Incidental Finding of Mucinous Colon Cancer by (18)F-Choline PET/CT Determining a Change in Clinical Management of a Patient with Recurrent Prostate Adenocarcinoma. Case Rep Oncol Med. 2014; 2014: 297031, doi: 10.1155/2014/297031, indexed in Pubmed: 25197590.
27. Hodolic M, Huchet V, Balogova S, et al. Incidental uptake of (18)F-fluoro-choline (FCH) in the head or in the neck of patients with prostate cancer. Radiol Oncol. 2014; 48(3): 228–234, doi: 10.2478/raon-2013-0075, indexed in Pubmed: 25177236.
28. Calabria F, Chiaravalloti A, Cicciò C, et al. PET/CT with 18 F-choline: Physiological whole bio-distribution in male and female subjects and diagnostic pitfalls on 1000 prostate cancer patients: 18 F-choline PET/CT bio-distribution and pitfalls. A southern Italian experience. Nucl Med Biol. 2017; 51: 40–54, doi: 10.1016/j.nucmedbio.2017.04.004, indexed in Pubmed: 28575697.
29. Pieterman RM, Que TH, Elsinga PH, et al. Comparison of (11)C-choline and (18)F-FDG PET in primary diagnosis and staging of patients with thoracic cancer. J Nucl Med. 2002; 43(2): 167–172, indexed in Pubmed: 11850480.
30. Giovacchini G, Giovannini E, Leoncini R, et al. PET and PET/CT with radiolabeled choline in prostate cancer: a critical reappraisal of 20 years of clinical studies. Eur J Nucl Med Mol Imaging. 2017; 44(10): 1751–1776, doi: 10.1007/s00259-017-3700-x, indexed in Pubmed: 28409220.