Diagnostic performance of a streamlined Fluorine-18 Choline PET-CT protocol for detection of prostate carcinoma recurrence in combination with appropriate-use criteria

Russell Frood[1], James Baren[1], Garry McDermott[2], David Bottomley[3], Chirag Patel[1], Andrew Scarsbrook[1, 4]

1. Department of Nuclear Medicine, Leeds Teaching Hospitals NHS Trust, UK
2. Department of Medical Physics & Engineering, Leeds Teaching Hospitals NHS Trust, UK
3. Department of Oncology, Leeds Teaching Hospitals NHS Trust, UK
4. Leeds Institute of Cancer and Pathology, University of Leeds, UK

Corresponding Author:

Dr Russell Frood, Research Fellow, Department of Nuclear Medicine, Level 1, Bexley Wing

St James's University Hospital, Beckett Street, Leeds, LS9 7TF, United Kingdom

Tel: +441132068212

Fax: +441132068228

Email: russellfrood@nhs.net

Running title: Efficacy of streamlined 18-F Choline PET-CT

Highlights

1. Choline PET/CT remains a useful tool for the detection of prostate cancer recurrence.
2. The sensitivity of choline PET/CT to detect recurrence can be improved by using appropriate use criteria.
3. Removal of dynamic and delayed acquisition phases reduces study time without adversely affecting accuracy.

Abstract

Purpose: To evaluate the efficacy of single time-point whole-body Fluorine-18 Choline PET-CT compared to a triple-phase acquisition protocol in the detection of prostate carcinoma recurrence.

Materials and Methods: Consecutive Choline PET-CT studies performed at a single tertiary referral centre in patients with biochemical recurrence of prostate carcinoma between September 2012 and March 2017 were retrospectively reviewed. The indication for the study, scanning protocol used, imaging findings, whether management was influenced by the PET-CT and subsequent patient outcome were recorded.

Results: 91 scans were performed during the study period; 42 were carried out using a triple-phase scanning protocol (dynamic pelvic imaging for 20 minutes after tracer injection, half-body acquisition at 60 minutes and delayed pelvic scan at 90 minutes) between 2012 and August 2015. Subsequently following interim review of diagnostic performance, a streamlined protocol and appropriate-use criteria were introduced. 49 scans were carried out using the single-phase scanning protocol between 2015 and 2017. 29 (69%) of the triple-phase studies were positive for recurrence compared to 38 (78%) of the single-phase studies. Only one patient who had a single-phase study would have benefited from

a dynamic acquisition, they have required no further treatment or imaging and are currently under PSA surveillance.

Conclusion: Choline PET-CT remains a useful tool for the detection of prostate recurrence when used in combination with appropriate-use criteria. Removal of dynamic and delayed acquisition phases reduces study time without adversely affecting accuracy. Benefits include shorter imaging time which improves patient comfort, reduced cost and improved scanner efficiency.

Introduction

Prostate carcinoma is the second most common malignancy affecting men worldwide with 1.7 million new cases expected by 2030 if the current trend continues.[1] A third of patients develop recurrence following radical treatment.[1] Positron emission tomography – computed tomography (PET-CT) is not routinely used in the initial work up of patients with suspected prostate malignancy but has been demonstrated to have, in a meta-analysis by Evangelista et al., a pooled sensitivity of 49.2% (95% CI: 39.9%-58.4%) and specificity of 95% (95% CI: 92.0% -97.1%) for the initial staging of lymph nodes.[2] The use of PET-CT has become more widely accepted in the investigation of patients with biochemical recurrence. There is evidence for the use of multi-parametric magnetic resonance imaging (mpMRI), which can aid in the detection of local recurrence, however, PET-CT allows both local recurrence and distant metastases to be identified.[3] There is an established role for Choline PET-CT in patients who have undergone radical treatment and have evidence of biochemical failure (rising prostate specific antigen, PSA), when there is negative or equivocal conventional imaging and the patient is suitable for further salvage treatment.[4,5] Choline accumulates in tumours which have a low glucose metabolism as it is an analogue for the biosynthesis of the cell membrane.[6, 7, 8, 9] The sensitivity and specificity of Choline PET-CT for detecting all sites of recurrence has been reported to be 85.6% (95% CI: 82.9%–88.1%) and 92.6% (95% CI: 90.1%–94.6%), respectively.[10]

A rapid PSA doubling time (< 6 months), increasing PSA level despite androgen deprivation therapy, PSA >2 ng/ml, a high Gleason score or high PSA nadir after radical prostatectomy increase the likelihood of a positive Choline PET-CT study.[11, 12, 13]

Choline PET-CT has traditionally been performed using a triple-phase scanning protocol, however, there is no universally agreed protocol with centres performing either a triple-phase protocol or a variation where either the delayed or dynamic phase is excluded. During the triple-phase protocol,

patients have an early dynamic acquisition through the pelvis, followed by a standard half-body scan from skull base to upper thighs 60 minutes after tracer injection and a delayed pelvic acquisition. The rationale for this protocol is firstly to differentiate tracer uptake within the prostate from physiological urinary accumulation and secondly to determine the uptake characteristics of lymph nodes to aid in classification between benign or malignant pathologies.[14, 15, 16, 17] This, however, does mean that patients spend a longer time within the department which is inconvenient and reduces patient throughput.

More recently the use of prostate specific membrane antigen (PSMA) PET-CT has been reported to have greater sensitivity in the detection of prostate carcinoma when compared to Choline PET-CT.[18] However, this is not currently funded by NHS England and is only available in very few centres in the United Kingdom. There is also a paucity of cost-effectiveness data supporting the widespread transition to this technique. Use of Choline PET-CT in this clinical scenario is however, in the list of indications funded by NHS England and more readily available at a range of specialist centres across England. For the foreseeable future in the UK, there is still likely to be a valuable role for Choline PET-CT in the detection of site of recurrence and formation of management plans.

The purpose of this study was to evaluate the utility of a streamlined (single-phase) scanning protocol for Choline PET-CT as part of a quality improvement process and secondly to review the positive detection rate of Choline PET-CT using appropriate-use criteria at our institution in comparison to published data.

Methods

A retrospective review of consecutive Choline PET-CT studies undertaken at a single institution between September 2012 and March 2017 was performed. The indication for the study, scanning protocol used, imaging findings, whether management was influenced by the PET-CT and patient outcome were all recorded.

Appropriate Use Criteria

Referring clinicians were provided with appropriate use criteria for Choline PET-CT referrals which included:

1. Assessment of patients with biochemical relapse after prior local treatment with curative intent (radical prostatectomy, radiotherapy or brachytherapy) to differentiate between local, loco-regional and systemic relapse;
2. Serum PSA > 1 ng/mL and results of the scan will influence patient management e.g. salvage radiotherapy or prostatectomy would be performed if localized recurrence is confirmed;
3. Studies are more likely to have a higher diagnostic utility if there is a high Gleason score, a rapid PSA doubling time (< 6 months), increasing PSA level despite androgen deprivation therapy or high PSA nadir after radical prostatectomy;
4. The study may not be clinically useful if the PSA is <2 ng/ml.

Appropriate use criteria were introduced at the time as the single-phase protocol.

Scanning Protocol

Triple-phase Acquisition

PET-CT was performed on a 64 slice Discovery 690 scanner (GE Healthcare, Waukesha, Wisconsin, USA). 4 MBq per kilogram of body mass of Fluorine-18 Ethyl-Choline was injected intravenously. A dynamic single bed position list mode study was acquired through the pelvis from 0 to 20 minutes following injection. At 60 minutes PET images were acquired from skull base to upper thighs. Finally, a delayed single bed position pelvic PET was performed at 90 minutes. Low-dose, unenhanced CT was also performed: 140 kV; 80 mAs; tube rotation time 0.5s per rotation; pitch 6; 3.75 mm slices (matching PET slice thickness). Patients maintained shallow respiration during the examination. Images were reconstructed using a standard ordered subset expectation maximization (OSEM) algorithm with CT used for attenuation correction. Both non-attenuation corrected and attenuation corrected datasets were reconstructed.

Single-phase Acquisition

PET-CT performed on one of 2 64 slice scanners Discovery 690 and Discovery 710 (GE Healthcare). A fixed dose of 350MBq of Fluorine-18 Ethyl-Choline was injected intravenously. At 60 minutes PET images were acquired from skull base to upper thighs. Low-dose, unenhanced CT was also performed: 140 kV; 80 mAs; tube rotation time 0.5s per rotation; pitch 6; 3.75 mm slices (matching PET slice thickness). Patients maintained shallow respiration during the examination. Images were reconstructed using a standard ordered subset expectation maximization (OSEM) algorithm with CT used for attenuation correction. Both non-attenuation corrected and attenuation corrected datasets were reconstructed.

Image Interpretation

Images were retrospectively reviewed independently by two dual-trained Consultant Radiologists & Nuclear Medicine Physicians with at least 8 years' experience of PET-CT interpretation, using specialised software (Advantage Windows Version 4.5, GE Healthcare). The scans were evaluated qualitatively and quantitatively (using maximum standardised uptake value (SUVmax)). If the study was performed using triple-phase protocol the dynamic and delayed acquisitions were rated on whether they contributed to scan interpretation on a per lesion and per patient basis independently and any disagreements were reviewed and agreed in consensus.

Data Analysis

PSA doubling time and PSA velocity were calculated using an online calculator available at http://www.doubling-time.com/compute-PSA-doubling-time.php. The difference in PSA, PSA velocity and PSA doubling time between negative and positive studies were analysed using Mann Whitney U tests. All statistical analysis was performed using IBM SPSS Statistics (Version 22, Armonk, New York, USA).

Results

84 patients were scanned during the study period. Mean patient age was 68 years (range 48 - 80 years). 91 Choline PET-CT scans were performed, most were carried out following rising PSA post treatment (n= 82) (**Table 1**). Pre-scan PSA values were available for 76 patients. The median pre-scan PSA value was 2.58ng/ml (range 0.06 - 147ng/ml), the median time from last PSA to Choline PET-CT was 40.5

days (range 2 to 188 days), the median PSA doubling time was 0.51 years (range -0.96 - 12.2ng/ml) and the median PSA velocity was 0.11ng/ml/month (range -3.62 - 1.48ng/ml/month).

There was a significant difference in PSA velocity for positive compared to negative studies, median 0.11ng/ml/month and 0.05 for positive and negative studies respectively, ($p = 0.038$) and pre-test PSA 3.2ng/ml and 1.3ng/ml for positive and negative scans respectively, ($p=0.002$). There was no significant difference in PSA doubling time between positive and negative studies.

42 (46%) Choline PET-CT studies were carried out using the triple-phase scanning protocol. Of these, 29 (69%) studies were positive for recurrence: 11 local recurrence, 10 nodal relapse and 8 with distant metastases. One study benefited from the dynamic acquisition (**Figure 1**) and one study benefited from either the dynamic or delayed acquisition (**Figure 2**). Four patients who had a triple-phase study had equivocal findings on Choline PET-CT **(Table 2)**. Of these, two had biopsy proven metastases, one patient was started on hormone and radiotherapy treatment because of the PET-CT and one patient underwent an MRI to evaluate equivocal bone uptake which did not demonstrate a metastasis (**Figure 3**), the patient remains disease free following 3 years of follow up.

49 (54%) studies were performed using the single-phase acquisition protocol. Of these studies, 38 (78%) were positive for recurrence; 10 demonstrating local recurrence, 3 local and nodal disease, 16 nodal disease, 7 with distant metastases and 2 with local, nodal and metastases. Five patients who had a single-phase study had indeterminate findings on the PET-CT. Of these patients, one patient was felt to have possible prostatitis but was later proven to have local recurrence, two patients were put into a surveillance programme, one patient was started on hormone therapy and one patient with indeterminate bone lesions was found to have had previous trauma to the areas after clinical correlation (**Table 2**). Only one of these patients would have benefited from an early dynamic

acquisition as they had a focus of activity within the central prostate, which was felt to represent physiological urinary activity within the prostatic urethra (**Figure 4**). They are currently having surveillance PSAs with the plan to start hormonal treatment if the PSA continues to rise. One patient had two negative Choline PET-CT studies although his PSA was continuing to rise (PSA 0.35ng/ml on initial imaging and 3.5ng/ml at the time of the second study, PSA velocity = 0.02 ng/ml/month) with the plan for PSA surveillance and hormone therapy if the PSA continued to increase.

The PSA levels of patients with negative or positive studies were not significantly different between the single or triple-phase protocols (p=0.501 and p=0.163 respectively) (**Figure 5**). There were six scans which were performed using the single-phase protocol which had a PSA of <1ng/ml, three of which were positive. Two of these patients did however have high PSA doubling times <6 months. Seven of the patients who had triple-phase studies had PSA levels of less than 1ng/ml, four of which were negative. All the triple-phase study patients with PSA <1ng/ml had PSA doubling times <6 months.

Discussion

In other developed nations, Choline PET-CT use in the evaluation of patients with prostate cancer is being gradually eclipsed by more sensitive PET tracers targeting PSMA.[19] PSMA imaging does have some limitations due to PSMA expression not being limited to the prostate, as its name would imply, and also there is currently a lack of evidence demonstrating its effect on patient outcome in early biochemical recurrence.[20] In addition, the amino acid PET tracer, 18F-Fluciclovine, recently approved for recurrent prostate cancer imaging, is injected with a short uptake time with relatively low urinary bladder activity, circumventing some of the issues posed with the logistics and interpretation of choline scans.[21] For a variety of economic and logistical reasons these tracers are not currently funded by the National

Health Service in the UK. However, there is established funding and infrastructure for Choline PET-CT at several specialist centres in England. This study has confirmed that Choline PET-CT remains a useful tool in the detection of prostate carcinoma recurrence particularly when used in conjunction with appropriate use criteria. Overall 67 of 91 (74%) of studies were positive for recurrence and rationalisation of the technique to a single-phase protocol did not lead to a reduction in positive rate (78%). A recent meta-analysis incorporating 18 studies with a combined 2,126 participants reported a pooled detection rate for Choline PET-CT in prostate cancer of 62% (95% CI 53%-93%).[22] The difference in the detection rate is likely due to the variations in referral criteria and clinical indication as it has previously been demonstrated that Choline PET-CT studies are more likely to be positive when there is rapidly doubling PSA or the PSA is rising despite androgen therapy.[23, 24] There was no significance in PSA doubling times between positive and negative scans in this study but there was a statistically significant difference when comparing PSA velocities and pre-test PSA values for patients with positive studies when compared with negative ones. The lack of significance in PSA doubling time is likely due to the relatively small patient cohort combined with the fact that 50% of patients with a PSA doubling time of less than a year have been reported to have recurrence which all leads to a degree of error.[23] However, this study does highlight the relatively high detection rate if appropriate use criteria are used.

The utility of dynamic and delayed imaging has been reported by a number of previous studies in the detection of local and distant disease.[14, 15, 16, 17, 25, 26] Other groups have reported using a single-phase acquisition protocol but with lower positive detection rates than in this study (42.9% - 62%).[27,28] The variation in the positive detection rates likely reflects the usefulness of appropriate use criteria in patient selection. Three of the 91 PET-CT studies (3%) performed in our cohort may have benefited from an extra acquisition to differentiate between pathological and physiological uptake, only one of these was a patient who had a single-phase acquisition study. This scan was reported as likely

physiological urinary activity within the central prostate and therefore the patient was managed conservatively with PSA surveillance. The PSA remained stable and it was concluded that the uptake was physiological.

Even if a PET-CT is negative further management can still be derived. One patient had two negative PET-CTs but the PSA was continuing to rise (PSA 0.35ng/ml on initial imaging and 3.5ng/ml at the time of the second study, PSA velocity = 0.02 ng/ml/month) and therefore was started on hormonal treatment as it was felt that the Choline study missed recurrence. This did not have a negative impact on the long-term prognosis of the patient. Their PSA remained stable following hormonal treatment and there was no further indication of recurrence. In the future, if limited funding becomes available for PSMA PET-CT, a sequential imaging approach could be adopted with Choline PET-CT used first-line and PSMA PET-CT reserved for negative cases.[29]

Limitations of this study include the retrospective nature, relatively small cohort size and lack of histological validation for the examinations that are reported as positive as not all patients had salvage surgery to provide histological evidence of recurrence.

Despite the stated limitations this study has confirmed that streamlining the PET-CT scanning protocol from three- to single-phase acquisition reduced study time without adversely affecting accuracy. The single-phase protocol has reduced scanning time by approximately a half (from 60 minutes to 30 minutes), this facilitates increased scanner throughput. More importantly, adherence to appropriate use criteria results in a higher detection rate than in prior published series. This quality improvement process has added benefits of reduced patient inconvenience, decreased overall cost and improved scanner efficiency.

Conclusion

Choline PET-CT remains a useful tool for the detection of prostate recurrence when used in combination with appropriate-use criteria. Removal of dynamic and delayed acquisition phases reduces study time without adversely affecting accuracy. Benefits include less patient inconvenience, reduced cost and improved scanner efficiency.

References

1 Han M, Partin AW, Pound CR, Epstein JI, Walsh PC. Long-term biochemical disease-free and cancer-specific survival following anatomic radical retropubic prostatectomy. The 15-year Johns Hopkins experience. Urol Clin North Am 2001; 28(3): 555-565.

2 Evangelista L, Guttilla A, Zattoni F, Muzzio PC. Utility of choline positron emission tomography/computed tomography for lymph node involvement identification in intermediate- to high-risk prostate cancer: a systematic literature review and meta-analysis. Eur Urol 2013;63:1040-8.

3Woodrum DA, Kawashima A, Gorny KR, Mynderse LA. Prostate cancer: state of the art imaging and focal treatment. Clin Radiol 2017; 72(8): 665-679.

4 Mottet N, Bellmunt J, Bolla M, et al. EAU guidelines on Prostate Cancer. Part 2: Treatment of advanced, relapsing, and castration-resistant prostate cancer. Eur Urol 2014; 65: 467-479.

5 Royal College of Radiologists, Royal College of Physicians of London, Royal College of Physicians and Surgeons of Glasgow, Royal College of Physicians of Edinburgh, British Nuclear Medicine Society, Administration of Radiactive Substances Advisory Committee. Evidence-based indications for the use of PET-CT in the United Kingdom 2016. Clin Radiol 2016; 71(7): e171-e188.

6 Hara T, Kosaka N, Kishi H. Development of (18)F-fluoroethylcholine for cancer imaging with PET: synthesis, biochemistry, and prostate cancer imaging. J Nucl Med 2002; 43(2): 187-199.

7 Price DT, Coleman RE, Liao RP. Comparison of [18 F]fluorocholine and [18 F]fluorodeoxyglucose for positron emission tomography of androgen dependent and androgen independent prostate cancer. J Urol 2002; 168(1): 273-280.

8 Hara T, Bansal A, DeGrado TR. Effect of hypoxia on the uptake of [methyl-3H]choline, [1-14C] acetate and [18F]FDG in cultured prostate cancer cells. Nucl Med Biol 2006; 33(8): 977-984.

9 Hofer C, Laubenbacher C, Block T, Breul J, Hartung R, Schwaiger M. Fluorine-18-fluorodeoxyglucose positron emission tomography is useless for the detection of local recurrence after radical prostatectomy. Eur Urol 1999; 36: 31–35.

10 Evangelista L, Zattoni F, Guttilla A, et al. Choline PET or PET/CT and biochemical relapse of prostate cancer: a systematic review and meta-analysis. Clin Nucl Med 2013; 38(5): 305-314.

11 Castellucci P, Fuccio C, Nanni C, et al. Influence of trigger PSA and PSA kinetics on 11C-Choline PET/CT detection rate in patients with biochemical relapse after radical prostatectomy. J Nucl Med 2009; 50(9): 1394–1400. Erratum in: J Nucl Med 2009; 50(10): 1578.

12 Beheshti M, Haim S, Zakavi R, et al. Impact of 18F-Choline PET/CT in Prostate Cancer Patients with Biochemical Recurrence: Influence of Androgen Deprivation Therapy and Correlation with PSA Kinetics. J Nucl Med 2013; 54: 833-840.

13 Cimitan M, Evangelista L, Hodolic M, et al. Gleason score at diagnosis predicts the rate of detection of 18F-choline PET/CT preformed when biochemical evidence indicates recurrence of prostate cancer: experience with 1,000 patients. J Nucl Med 2015; 56(2): 209-215.

14 Steiner C, Vees H, Zaidi H, et al. Three-phase 18F fluorocholine PET/CT in the evaluation of prostate cancer recurrence. Nuklearmedizin 2009; 48: 1-9.

15 Beheshti M, Haim S, Zakavi R, et al. Impact of 18F-choline PET/CT in prostate cancer patients with biochemical recurrence: influence of androgen deprivation therapy and correlation with PSA kinetics. J Nucl Med 2013; 54: 833-840.

16 DeGrado TR, Baldwin SW, Wang S, Orr MD, Liao RP, Friedman HS, et al. Synthesis and evaluation of (18)F-labeled choline analogs as oncologic PET tracers. J Nucl Med 2001; 42: 1805-1814.

17 Kumar R, Dhanpathi H, Basu S, Rubello D, Fanti S, Alavi A. Oncologic PET tracers beyond [(18)F]FDG and the novel quantitative approaches in PET imaging. Q J Nucl Med Mol Imaging 2008; 52: 50–65.

18 Schwenck J, Rempp H, Reischl G, Kruck S. Comparison of 68Ga-labelled PSMA-11 and 11C-choline in the detection of prostate cancer metastases by PET/CT. Eur J Nucl Med Mol Imaging 2017; 44(1): 92-101.

19 von Eyben FE, Picchio M, von Eyben R, Rhee H, Bauman G. 68Ga-Labeled Prostate-specific Membrane Antigen Ligand Positron Emission Tomography/Computed Tomography for Prostate Cancer: A Systematic Review and Meta-analysis. Eur Urol Focus. 2016 Nov 15. pii: S2405-4569(16)30160-2. doi: 10.1016/j.euf.2016.11.002. [Epub ahead of print].

20 Hofman MS, Hicks RJ, Maurer T, Eiber M. Prostate-specific Membrane Antigen PET: Clinical Utility in Prostate Cancer, Normal Patterns, Pearls, and Pitfalls. Radiographics 2018; 38(1): 200-217.

21 Schuster DM, Nanni C, Fanti S, et al. Anti-1-amino-3-18F-fluorocyclobutane-1-carboxylic acid: physiologic uptake patterns, incidental findings, and variants that may simulate disease. J Nucl Med 2014; 55(12): 1986-1992.

22 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: 55-69.

23 Giovacchini G, Picchio M, Scattoni V, et al. PSA doubling time for prediction of [(11)C]choline PET/CT findings in prostate cancer patients with biochemical failure after radical prostatectomy. Eur J Nucl Med Mol Imaging 2010; 37(6): 1106-1116.

24 Chiaravalloti A, Di Biagio D, Tavolozza M, Calabria F, Schillaci O. PET/CT with (18)F-choline after radical prostatectomy in patients with PSA≤2 ng/ml. Can PSA velocity and PSA doubling time help in patient selection? Eur J Nucl Med Mol Imaging 2016; 43(8): 1418-1424.

25 Simone G, Di Pierro GB, Papalia R. Significant increase in detection of prostate cancer recurrence following radical prostatectomy with an early imaging acquisition protocol with ^{18}F-fluorocholine positron emission tomography/computed tomography.World J Urol 2015; 33(10): 1511-1518.

26 Chondrogiannis S, Marzola MC, Grassetto G, et al. New acquisition protocol of 18F-choline PET/CT in prostate cancer patients: review of the literature about methodology and proposal of standardization. Biomedical Res Int 2014; 2014: 215650 doi: 10.1155/2014/215650. Epub 2014 Jul 10.

27 E. Pelosi, V. Arena, A. Skanjeti, et al. Role of whole-body 18F-choline PET/CT in disease detection in patients with biochemical relapse after radical treatment for prostate cancer. Radiologia Medica 2008; 113(6): 895–904.

28 V. Graute, N. Jansen, C. Übleis, et al. Relationship between PSA kinetics and [18F]fluorocholine PET/CT detection rates of recurrence in patients with prostate cancer after total prostatectomy. Eur J Nucl Med Mol Imaging 2012; 39(2): 271–282.

29 Bluemel C, Krebs M, Polat B, et al. 68Ga-PSMA-PET/CT in Patients with Biochemical Prostate Cancer Recurrence and Negative 18F-Choline-PET/CT. Clin Nucl Med 2016; 41(7): 515-521.

Tables

Indication	Number of studies
Previous radical treatment and now rising PSA	82
Lesion detected on initial staging, PET-CT to clarify if only site of metastases	4
Lesion detected on repeat imaging, PET-CT to clarify if only site of metastases	4
Follow up of previously demonstrated tracer update on PET-CT	1

Table 1: Indications given on the requests for Choline PET-CT

Patient	Indication	PET-CT Finding	Outcome
1	Gleason 7. Previous radical radiotherapy. PSA rising	Diffuse prostate uptake - suspected prostatitis	MRI demonstrated recurrence
2	Brachytherapy and radiotherapy. PSA rising	Focus of activity in the central prostate likely urinary. Suspicious iliac chain nodes	PSA surveillance
3	Brachytherapy and radiotherapy. PSA rising	Suspicious for small-volume nodal recurrence within left common iliac, internal iliac and pelvic sidewall lymph nodes.	Hormone Therapy
4	Post prostatectomy and salvage radiotherapy. Rising PSA	Equivocal left external iliac lymph node with faint uptake	CT surveillance
5T	Lung metastasis resected. Now single metastasis in right posterior 7th rib. Query further sites of disease	Indeterminate mediastinal nodal tracer uptake	EBUS demonstrated metastatic lymph node
6T	Post prostatectomy and pelvic radiotherapy. Rising PSA	Probable localised recurrence within a solitary left pelvic sidewall node	Hormone treatment and radiotherapy
7T	Brachytherapy and radiotherapy for prostate cancer. Rising PSA	Possible early nodal recurrence within sub-cm right pelvic sidewall nodes	Lymphadenectomy - metastatic nodes
8	Sclerotic rib lesions on bone scan.	Tracer avid prostate cancer. The tracer negative rib lesions are indeterminate	Rib lesions due to previous trauma
9T	Post prostate brachytherapy. Rising PSA	Indeterminate focal uptake in the region of the right lesser trochanter – MR advised	MRI - No metastasis

Table 2: Indications and patient outcomes for equivocal findings on Choline PET-CT. Key: T= Triple-phase, EBUS = Endobronchial Ultrasound

Figures & Legends

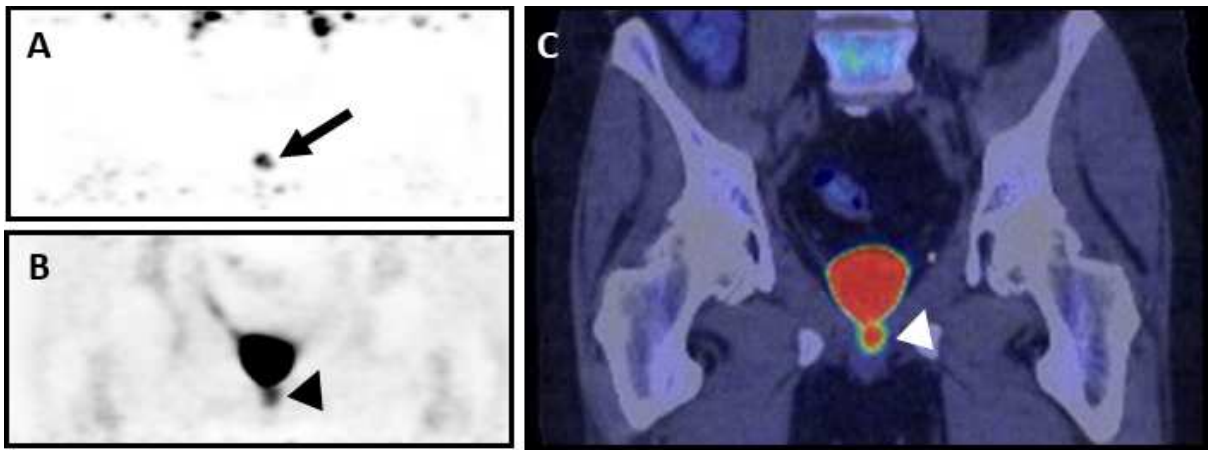

Figure 1: 18F-Choline PET-CT study of a 64 year old patient, who had previously been treated with a radical prostatectomy, with suspected recurrent prostate carcinoma. The dynamic study demonstrates a focus of uptake within the region of the prostate (A) (arrow), this is demonstrated before accumulation of tracer within the urinary bladder as demonstrated on the 60 minute acquisition (B) and fused PET-CT (C) (arrowheads). Therefore, this confirms the presence of local recurrence.

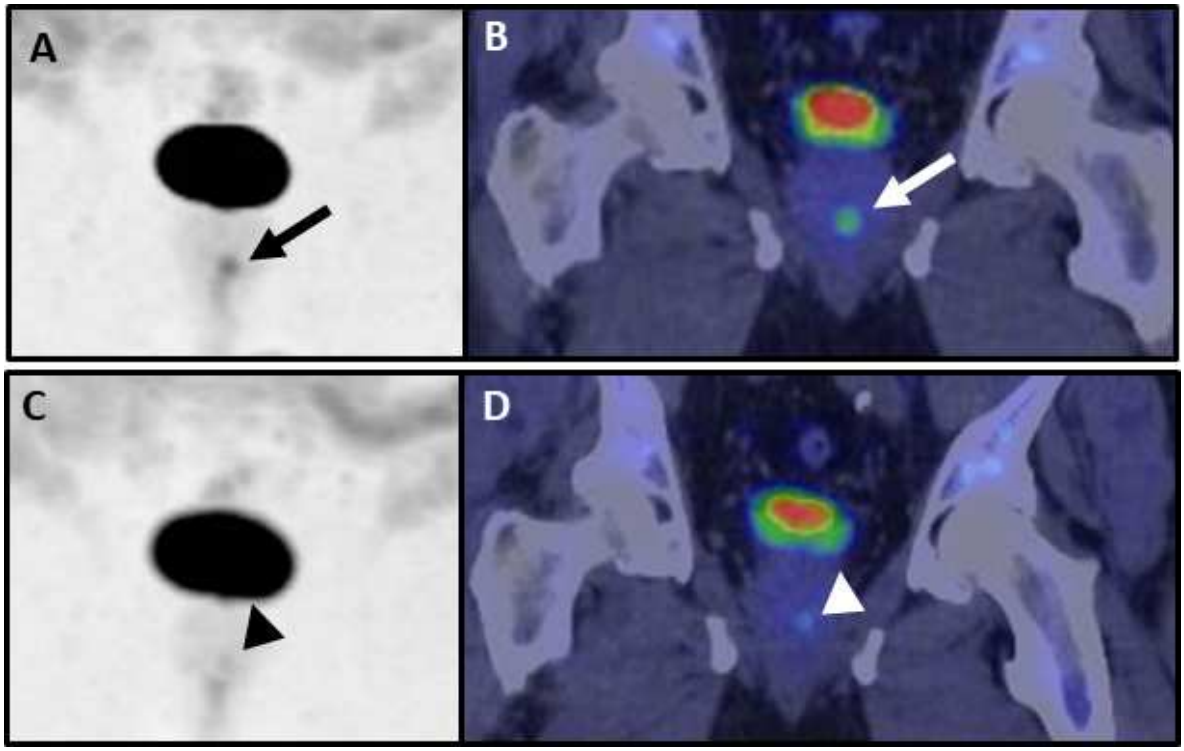

Figure 2: 18F-Choline PET-CT study of a 69 year old patient with suspected recurrent prostate carcinoma. The 60 minute coronal PET and fused PET-CT images demonstrate a focus of uptake within the region of the prostate (A and B) (arrows). This is demonstrated to washout on the delayed 90 minute coronal PET and fused coronal PET-CT (C and D) images (arrowheads) and therefore is likely physiological and not recurrence.

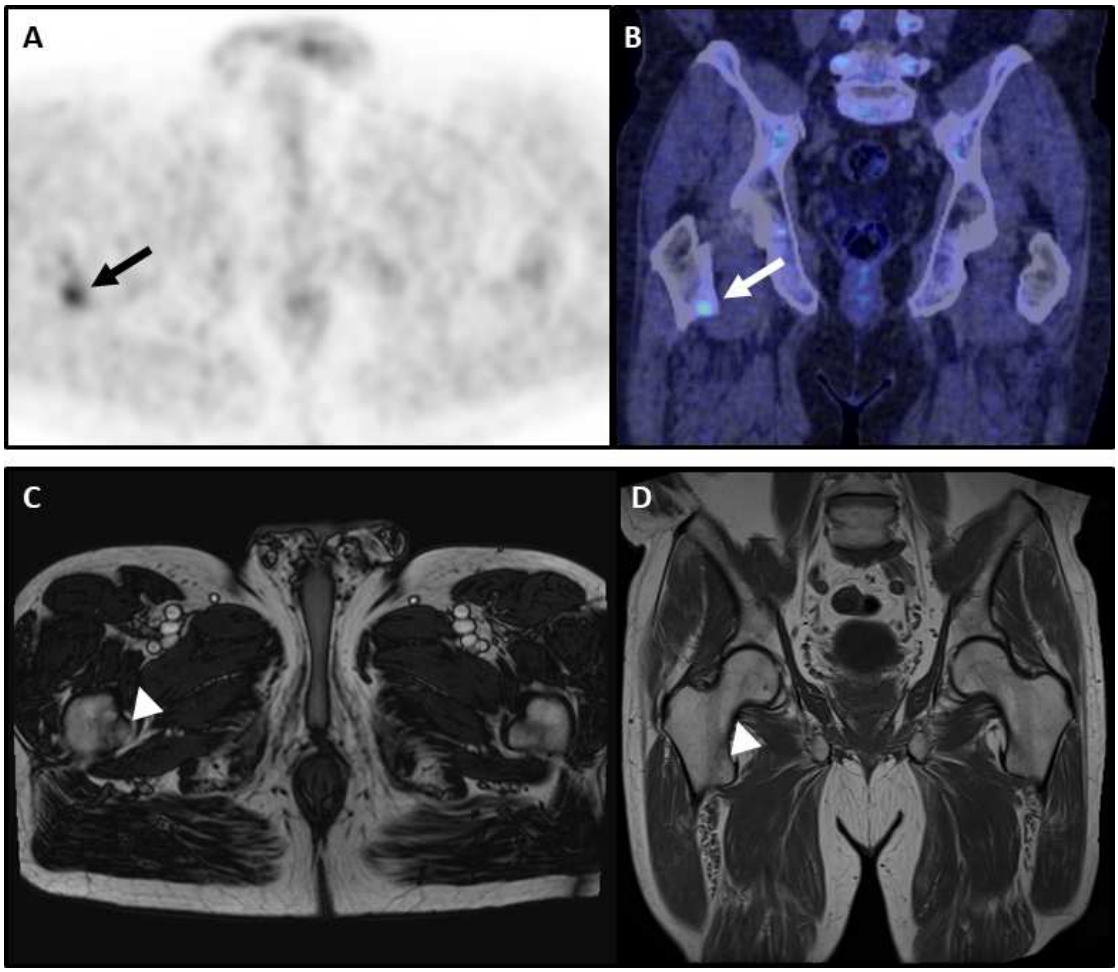

Figure 3: 18F-Choline PET-CT study of a 67 year old patient with suspected recurrent prostate carcinoma. The 60 minute single acquisition axial fused PET-CT (A) and coronal fused PET-CT (B) demonstrate a focus of tracer activity within the lesser trochanter of the left femur (arrows). Follow up imaging with MR demonstrates normal bone signal on T2 axial (C) and T1 coronal (D) sequences (arrowheads).

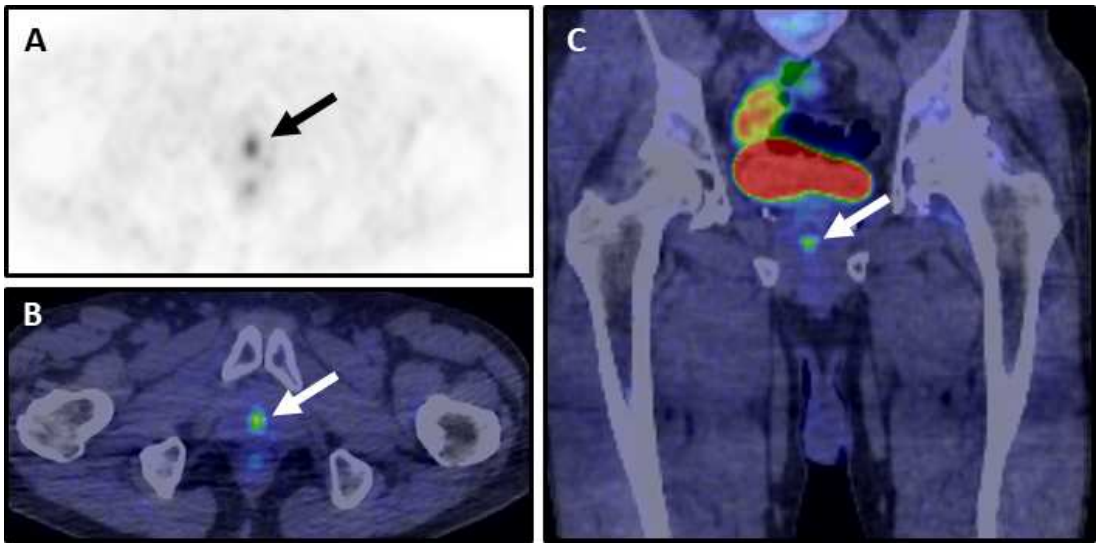

Figure 4: 18F-Choline PET-CT study of a 78 year old patient with suspected recurrent prostate carcinoma. The 60 minute single acquisition axial PET (A), axial fused PET-CT (B) and coronal fused PET-CT (C) images demonstrate a focus of activity within the central prostate (arrows), this was presumed to be from urinary activity.

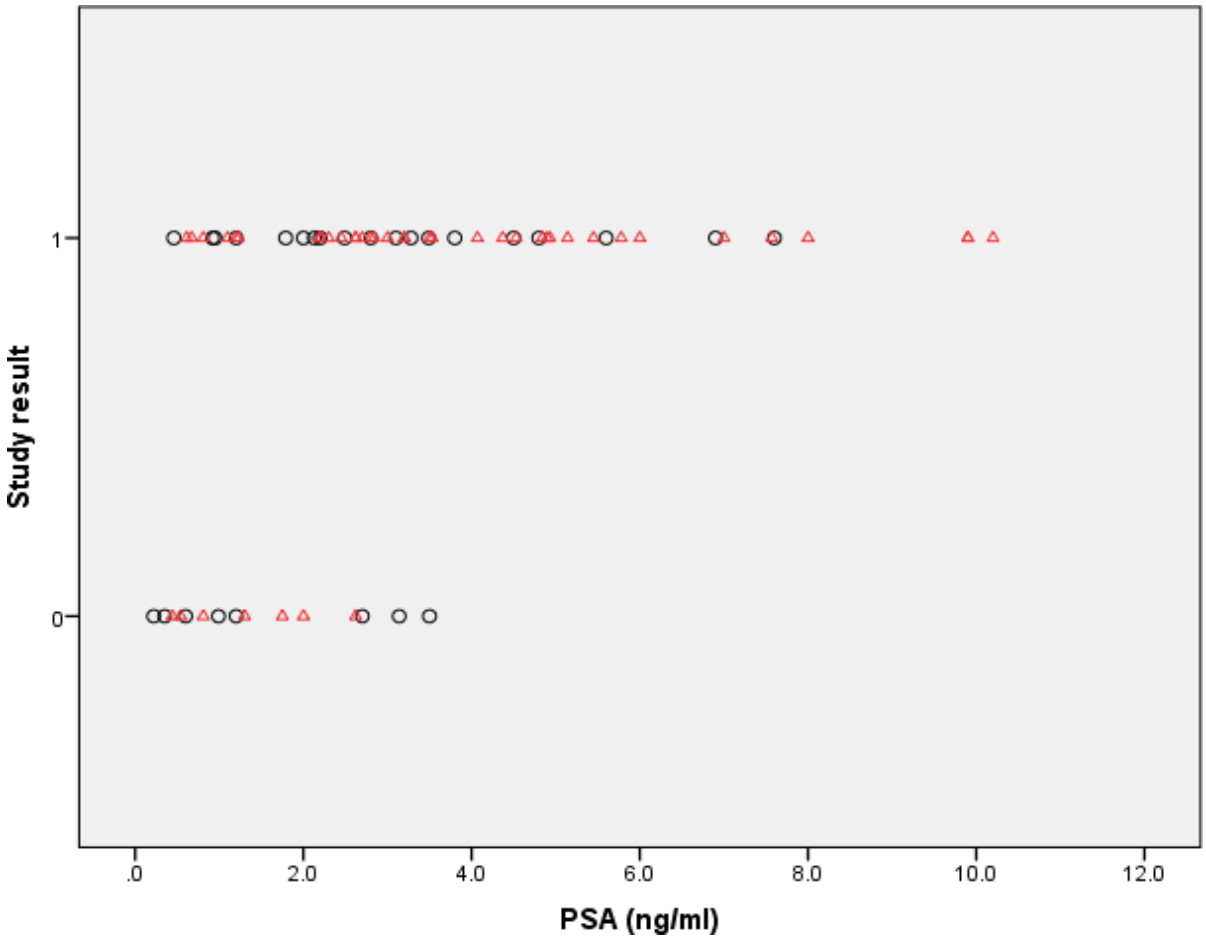

Figure 5: Comparison of the PSA levels for positive (1) and negative (0) studies between single-phase (triangles) and triple-phase studies (circles). Studies where the patient's PSA was over 12ng/ml were excluded, these were all positive scans.