

# Diagnostic value of bone scintigraphy for aseptic loosening after total knee arthroplasty

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## Abstract.

**BACKGROUND:** Despite technical improvements, aseptic loosening after total knee arthroplasty (TKA) remains a frequent complication. A one-stage revision arthroplasty is the most common therapeutic pathway.

**OBJECTIVE:** The aim of this study was to evaluate the diagnostic value of bone scintigraphy in detecting aseptic loosening after TKA.

**METHODS:** We retrospectively identified 46 cases of one-stage revision TKA performed between January 2011 and December 2012. In each case a bone scintigraphy was performed at least one year after the primary TKA and  $3.2 \pm 2.2$  month prior to revision arthroplasty. Additionally, we evaluated the rate of satisfaction and pain level  $16.2 \pm 5.4$  months after one-stage revision arthroplasty.

**RESULTS:** Bone scintigraphy indicated aseptic loosening in 28 cases. Intraoperative aseptic loosening was verified in 34 cases. Bone scintigraphy had a sensitivity of 0.76 and a specificity of 0.83 in detecting aseptic loosening. The positive predictive value was 0.93, and the negative predictive value 0.56. At follow-up consultation, 35 patients were very satisfied or satisfied, and 31 patients had no pain or occasional pain.

**CONCLUSIONS:** Bone scintigraphy is a helpful tool in detecting aseptic loosening after TKA. Nevertheless, the results from bone scintigraphy should be compared with clinical findings and patients' disorders.

**Level of evidence:** IV, retrospective study

Keywords: Aseptic loosening, one-stage revision arthroplasty, total knee arthroplasty

## 1. Introduction

Over the last two decades, the number of cases of total knee arthroplasty (TKA) for the treatment of osteoarthritis has been constantly growing. At the same time the total number of complications and revision surgery has also increased. Kurtz et al. reported a revision rate of 8% for all TKAs performed in the USA and aseptic loosening was cited as the most frequent reason for this [1]. Of all revisions, 23–71% were required because of aseptic loosening, 8.1–39% for instability, and 5–18.4% for infection [2–7]. Loosening of the tibial component, however, is more common than loosening of the femoral component [8]. Dalury et al. showed that aseptic loosening occurs rather late in the period after primary arthroplasty [5]. The detection of aseptic loosening still remains difficult [9–12].

The aim of this study was to describe the diagnostic value of bone scintigraphy in cases of assumed aseptic loosening after TKA.

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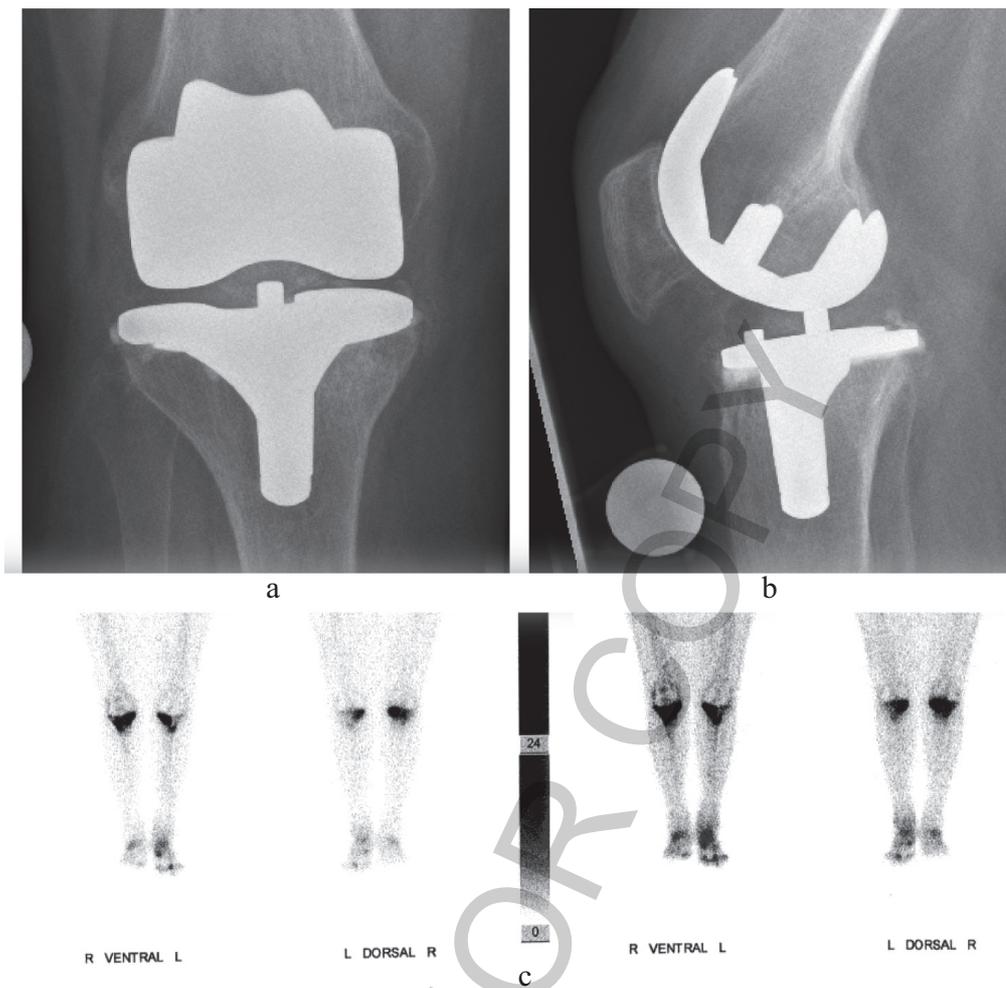


Fig. 1. Case description. A 66 year old patient developed pain of the right knee approximately 113 month after primary TKA. Pain was focused on the tibial plateau and increased through walking. Plain radiographs of this time presented no sure signs of an aseptic loosening or another pathology (a + b). There were no signs of an infection and no instability. The axis was normal. Bone scintigraphy was performed 115 month after TKA resulting in an aseptic loosening particularly of the tibial component (c). After one-stage revision arthroplasty of the right knee the patient had symptomatic improvement. As additional finding it occurred appearance of loosening of the TKA on the left knee. Because of a lack of clinical symptoms an operation was not indicated.

## 2. Patients and methods

We retrospectively analyzed 46 cases of one-stage revision arthroplasty performed between January 2011 and December 2012 in our institution. The mean age at time of operation was  $68.6 \pm 9.3$  years; 36 patients were female and 10 patients were male (Fig. 1). The inclusion criteria were diagnostic uncertainty after clinical and radiological examination, preoperative bone scintigraphy performed at least one year after primary TKA, and no loss to follow-up. The exclusion criterion was assumed or verified infection. The revision arthroplasty was performed  $74 \pm 59.7$  months after primary operation. The bone scintigraphy was performed  $3.2 \pm 2.2$  month prior to revision arthroplasty. All bone scintigraphies were conducted with three phases (perfusion phase, blood pool phase and late phase). In 24 cases tech-

netium 99m hydroxydiphosphonate was used, in 14 cases technetium 99m methylenediphosphonate was used and in eight cases technetium 99m hydroxymethylenediphosphonate. Owing to a diagnostic uncertainty including the differential diagnosis of a potential periprosthetic joint infection (PJI) a diagnostic aspiration was performed in six cases and a diagnostic arthroscopy in one case. Serum inflammatory parameters C-reactive protein (CRP) and serum white blood cell count (WBC) were assessed obligatory. The operations were performed under general or local anesthesia by seven senior surgeons of an own department specialized for revision arthroplasty. During each operation, samples were collected for microbiological and histological examination to exclude any infection. In ten cases one sample was collected, in eight cases two samples, in 18 cases three samples, in three cases four samples and in seven cases five samples. Initially, patients had a nerve block of the femoral nerve for three to four days to facilitate flexion. Further aftercare was identical in every case and consisted of full weight bearing with free range of motion.

Patients were contacted to evaluate their satisfaction and level of pain. The mean time of follow-up was  $16.2 \pm 5.4$  months. Patient responses were categorized as very satisfied, satisfied, partially satisfied, not satisfied or dissatisfied, and as no pain, occasional pain, moderate pain, daily pain and continuous severe pain.

Data collection and analysis were performed using GraphPad Prism 5 (GraphPad Software Inc., La Jolla, CA). The results were expressed with 95% confidence intervals.

The ethical committee of the Hannover Medical School approved the study.

### 3. Results

Bone scintigraphy revealed aseptic loosening in 28 cases. Intraoperatively, loosening of the prosthesis was visible in 34 patients. Revision arthroplasty was required for instability in ten cases, and in two cases for valgus deformity of the TKA without loosening or instability, but discomfort. The duration of the operation was  $153 \pm 56$  min. In 32 cases (69.6%), a non-constrained knee prosthesis was replaced with a partially constrained knee prosthesis, while in 14 cases (30.4%) a non-constrained knee prosthesis was replaced with a constrained knee prosthesis. Via preoperative diagnostic aspiration and diagnostic arthroscopy an infecting microorganism could not be verified. The CRP was elevated in three cases and independently WBC was elevated in five cases. Preoperative CRP had a value of  $0.39 \pm 0.39$  mg/dl, the preoperative value of WBC was  $7.2 \pm 2.2$ . In none of the cases with elevated CRP or WBC the clinical or intraoperative appearance indicated an infection. Intraoperative a microorganism was found in three cases (*Bacillus halodurans*, *Propionibacterium acnes*, *Staphylococcus cohnii cohnii*). In these three cases the microorganism could solely be verified in one of four (one case) or one of five (two cases) samples. Additionally preoperative serum inflammatory markers and clinical and intraoperative appearance were not suspect for an ongoing infection. Hence these verifications were classified as contamination in accordance with our institute for medical microbiology. Complications occurred in six patients (13%). Two patients each had two complications. An infection of the urinary tract appeared in two cases (4.3%). Major complications were deep vein thrombosis in three cases (6.5%) and a recurrent aseptic loosening in three cases (6.5%). The three patients with a recurrent aseptic loosening received another one-stage revision arthroplasty leading to a revision rate of 6.5%. During these revision procedures no infecting microorganism could be verified.

In the present study, the sensitivity of bone scintigraphy in detecting aseptic loosening after TKA was 0.76 (0.59–0.89) and the specificity was 0.83 (0.52–0.98). Furthermore, we found a positive and negative predictive value of 0.93 (0.77–0.99) and 0.56 (0.31–0.78), respectively.

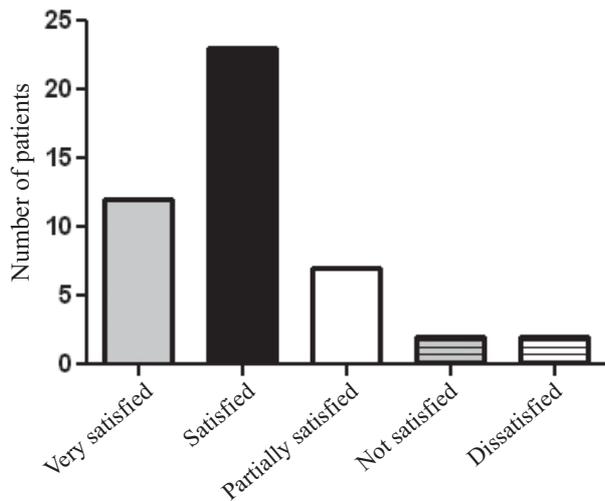


Fig. 2. Satisfaction. 12 patients were very satisfied and 23 satisfied. Two patients each were not satisfied or dissatisfied.

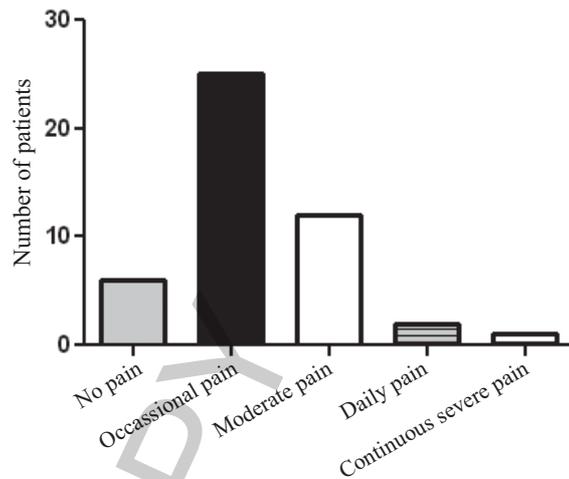


Fig. 3. Pain level. Two patients described daily pain at follow-up examination, one patient had continuous severe pain. Six patients had no pain, 25 patients had occasional pain.

At the follow-up consultation, 12 patients were very satisfied and 23 were satisfied. However, two patients each were not satisfied or dissatisfied (Fig. 2). Regarding pain at follow-up, six patients had no pain, 25 patients reported occasional pain and 12 patients moderate pain. Daily pain occurred in two patients, and one patient had continuous severe pain (Fig. 3).

#### 4. Discussion

The present study was performed to evaluate the diagnostic value of bone scintigraphy in cases of assumed aseptic loosening. We found high sensitivity, specificity and positive predictive value. Additionally, we described the outcome of one-stage revision arthroplasty in terms of satisfaction and pain, complications and revision rate.

There are several limitations to our study. One is its retrospective design. In addition, there are a limited number of cases, no control group and no standardized outcome parameters.

There are different opportunities treating aseptic loosening. We believe that a satisfactory specific conservative treatment has not yet been described. A common approach is symptomatic therapy via administration of antiphlogistics and analgesics, although research evidence is lacking. When conservative treatment fails, an operation is indicated. In cases of aseptic loosening, a one-stage revision arthroplasty is commonly performed. The literature describes the outcome after revision TKA as inferior to the outcome after primary TKA, underlined by higher complication and revision rates [5,13].

Despite an extensive literature review, we found no comparable data on patient-orientated outcome parameters such as satisfaction and pain levels after one-stage revision knee arthroplasty. Our results indicate that one-stage revision TKA leads to a high rate of satisfaction concurrently with a low pain level. Nevertheless, with four patients who were not satisfied and three patients with at least daily pain in a noteworthy number of cases, revision TKA does not necessarily lead to alleviated disorders. These results provide further evidence to inform patient choices. Thereby, informed consent for a planned one-stage revision arthroplasty is possible.

In contrast to our data, Gratz et al. described a negative predictive value of almost 1.0, whereas this value was the shortcoming of bone scintigraphy in our study, with a value of only 0.56 [9]. Klett reported a negative predictive value of 0.85, and a sensitivity value of 0.9 [8]. Smith described a sensitivity value of 0.92 and a negative predictive value of 0.95 [14]. The published data for sensitivity were similar to our own data, though the negative predictive value was reported to be higher. Bone scintigraphy is known to have a limited value within the first year after TKA owing to physiological biologic processes surrounding the prosthesis. In consequence, it shows positive results in asymptomatic patients [14,15]. Even two years after primary TKA, bone scintigraphy has reportedly shown an increased signal in 12.5% of asymptomatic patients [16]. Smith et al. recommend analyzing the trend of TKA uptake, and continue to question whether a definitive diagnosis of aseptic loosening is possible with only one scintigraphic study [14]. In the current study the duration between examination and operation of  $3.2 \pm 2.2$  month was deemed acceptable. This value is comparable to a study of Temmermann et al. [17]. Whereas a current examination prior to operation is desired there are influencing factors in daily practice leading to a delayed operation. Some patients obtain a second opinion; some patients initially refuse the operation. A cut off value for an acceptable duration between examination and operation is missing. Further costs and patients radiation load oppose the advantage of additional information of a further examination. This has to be discussed with the patient.

A PJI, including a low-grade infection, is a differential diagnosis for a painful knee after TKA [5]. Especially in cases of an assumed low-grade infection a remaining diagnostic uncertainty is possible [18]. In the present study we estimated serum inflammatory markers in every case, performed a diagnostic aspiration in six and a diagnostic arthroscopy in one case. Additionally we collected tissue samples during every operation. This represents the common diagnostic parameters for a PJI. Nevertheless their accuracy and thereby their diagnostic impact is a matter of discussion [2,19–21].

One disadvantage of bone scintigraphy is the lack of differentiation between septic and aseptic pathologies [14]; therefore, leukocyte scintigraphy is recommended. Simonsen et al. described a sensitivity of 0.81 and a specificity of 0.94 in detecting septic complications after total hip arthroplasty in leukocyte scintigraphy [15]. The combination of bone scintigraphy with leukocyte scintigraphy is reported to lead to more accurate diagnoses [9,15].

Positron emission tomography (PET) is considered to be an alternative to bone scintigraphy. Delank et al. described a sensitivity of 0.76 for 18-fluorodeoxyglucose PET ( $^{18}\text{F}$ -FDG PET) in detecting aseptic loosening compared with 0.75 for bone scintigraphy. Likewise, Sterner et al. reported a sensitivity of 1.0 and a specificity of 0.56 [22,23]. The values reported by Delank et al., for both PET and bone scintigraphy, were comparable to our own data for bone scintigraphy. However, in cases of septic complications, the sensitivity of PET was reported to be higher (1.0) [22]. Interestingly, Mayer-Wagner et al. described a lower degree of accuracy with  $^{18}\text{F}$ -FDG PET after TKA compared with  $^{18}\text{F}$ -FDG PET after total hip arthroplasty. They found a sensitivity of 0.56 for aseptic loosening and 0.14 for septic loosening [24]. These values for PET in septic and aseptic cases contradict those of Delank and colleagues. Therefore Mayer-Wagner et al. would not recommend using PET to diagnose aseptic loosening after TKA.

Nuclear arthrography is a further alternative to detect aseptic loosening. Temmermann et al. presented comparative data regarding bone scintigraphy and nuclear arthrography after hip arthroplasty. For cemented femoral components they described a sensitivity of 0.75 and a specificity of 0.67 for nuclear arthrography and a sensitivity of 0.89 and a specificity of 0.37 for bone scintigraphy. For uncemented femoral components again the sensitivity of bone scintigraphy was higher compared to nuclear arthrography and the specificity was lower. Additionally nuclear arthrography had a high interobserver agreement [17]. In a meta-analysis by Temmermann et al., bone scintigraphy was reported to be less accurate

in detecting aseptic loosening after total hip arthroplasty compared to plain radiographs and subtraction arthrography [25]. Contrastingly, the same study group described good interobserver reliability with bone scintigraphy compared to plain radiographs [17]. Ultimately, they recommended bone scintigraphy as an additional diagnostic tool for aseptic loosening. In a more recent study French et al. analyzed 27 patients after total hip or total knee arthroplasty that received a nuclear arthrography to detect aseptic loosening. They found a sensitivity of 0.93, a specificity of 0.83 and a positive and negative predictive value of 0.88 and 0.91 respectively [26]. The specificity and positive predictive value of bone scintigraphy of the present study is comparable to the values published by French et al. for nuclear arthrography. A disadvantage of nuclear arthrography might be the intraarticular injection regarding a risk of infection. Nevertheless it is an alternative with a high accuracy.

Treating complications after TKA remains difficult, both for the practitioner and for the patient. Accurate diagnoses are crucial for the successful treatment of complications. In this study, bone scintigraphy proved to be a useful tool in the detection of aseptic loosening after TKA.

### Conflict of interest

Each author certifies that he has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

### References

- [1] Kurtz S, Mowat F, Ong K, Chan N, Lau E, Halpern M. Prevalence of primary and revision total hip and knee arthroplasty in the United States from 1990 through 2002. *J Bone Joint Surg Am* 2005 Jul; 87(7): 1487-1497.
- [2] Parvizi J, Jacovides C, Zmistowski B, Jung KA. Definition of periprosthetic joint infection: Is there a consensus? *Clin Orthop Relat Res* 2011 Nov; 469(11): 3022-3030.
- [3] Mortazavi SM, Schwartzberger J, Austin MS, Purtill JJ, Parvizi J. Revision total knee arthroplasty infection: Incidence and predictors. *Clin Orthop Relat Res* 2010 Aug; 468(8): 2052-2059.
- [4] Bedair H, Ting N, Jacovides C, Saxena A, Moric M, Parvizi J, et al. The Mark Coventry Award: diagnosis of early postoperative TKA infection using synovial fluid analysis. *Clin Orthop Relat Res* 2011 Jan; 469(1): 34-40.
- [5] Dalury DF, Pomeroy DL, Gorab RS, Adams MJ. Why are Total Knee Arthroplasties Being Revised? *J Arthroplasty* 2013 Jul 22.
- [6] Labek G, Todorov S, Iovanescu L, Stoica CI, Bohler N. Outcome after total ankle arthroplasty-results and findings from worldwide arthroplasty registers. *Int Orthop* 2013 Jul 6.
- [7] Song SJ, Detch RC, Maloney WJ, Goodman SB, Huddleston JI, 3rd. Causes of Instability After Total Knee Arthroplasty. *J Arthroplasty* 2013 Jul 26.
- [8] Klett R, Steiner D, Laurich S, Bauer R, Kordelle J. Evaluation of aseptic loosening of knee prostheses by quantitative bone scintigraphy. *Nuklearmedizin* 2008; 47(4): 163-166.
- [9] Gratz S, Hoffken H, Kaiser JW, Behr TM, Strosche H, Reize P. Nuclear medical imaging in case of painful knee arthroplasty. *Radiologe* 2009 Jan; 49(1): 59-67.
- [10] Levitsky KA, Hozack WJ, Balderston RA, Rothman RH, Gluckman SJ, Maslack MM, et al. Evaluation of the painful prosthetic joint. Relative value of bone scan, sedimentation rate, and joint aspiration. *J Arthroplasty* 1991 Sep; 6(3): 237-244.
- [11] Miller TT. Imaging of knee arthroplasty. *Eur J Radiol* 2005 May; 54(2): 164-177.
- [12] Swiatkowski J. Diagnostics imaging of aseptic and septic loosening of hip joint prosthesis. *Ortop Traumatol Rehabil* 2001 Jan-Mar; 3(1): 6-10.
- [13] Baker P, Cowling P, Kurtz S, Jameson S, Gregg P, Deehan D. Reason for revision influences early patient outcomes after aseptic knee revision. *Clin Orthop Relat Res* 2012 Aug; 470(8): 2244-2252.
- [14] Smith SL, Wastie ML, Forster I. Radionuclide bone scintigraphy in the detection of significant complications after total knee joint replacement. *Clin Radiol* 2001 Mar; 56(3): 221-224.

- [15] Simonsen L, Buhl A, Oersnes T, Duus B. White blood cell scintigraphy for differentiation of infection and aseptic loosening: A retrospective study of 76 painful hip prostheses. *Acta Orthop* 2007 Oct; 78(5): 640-647.
- [16] Duus BR, Boeckstyns M, Stadeager C. The natural course of radionuclide bone scanning in the evaluation of total knee replacement – a 2 year prospective study. *Clin Radiol* 1990 May; 41(5): 341-343.
- [17] Temmerman OP, Raijmakers PG, Berkhof J, David EF, Pijpers R, Molenaar MA, et al. Diagnostic accuracy and inter-observer variability of plain radiography, subtraction arthrography, nuclear arthrography, and bone scintigraphy in the assessment of aseptic femoral component loosening. *Arch Orthop Trauma Surg* 2006 Jul; 126(5): 316-323.
- [18] Vasso M, Schiavone Panni A. Low-grade periprosthetic knee infection: diagnosis and management. *J Orthop Traumatol* 2014 May 14.
- [19] Kusuma SK, Ward J, Jacofsky M, Sporer SM, Della Valle CJ. What is the role of serological testing between stages of two-stage reconstruction of the infected prosthetic knee? *Clin Orthop Relat Res* 2011 Apr; 469(4): 1002-1008.
- [20] Schindler M, Christofilopoulos P, Wyssa B, Belaieff W, Garzoni C, Bernard L, et al. Poor performance of microbiological sampling in the prediction of recurrent arthroplasty infection. *Int Orthop* 2011 May; 35(5): 647-654.
- [21] Squire MW, Della Valle CJ, Parvizi J. Preoperative diagnosis of periprosthetic joint infection: role of aspiration. *AJR Am J Roentgenol* 2011 Apr; 196(4): 875-879.
- [22] Delank KS, Schmidt M, Michael JW, Dietlein M, Schicha H, Eysel P. The implications of 18F-FDG PET for the diagnosis of endoprosthetic loosening and infection in hip and knee arthroplasty: results from a prospective, blinded study. *BMC Musculoskelet Disord* 2006 Mar 3; 7: 20.
- [23] Sterner T, Pink R, Freudenberg L, Jentzen T, Quitmann H, Bockisch A, et al. The role of [18F]fluoride positron emission tomography in the early detection of aseptic loosening of total knee arthroplasty. *Int J Surg* 2007 Apr; 5(2): 99-104.
- [24] Mayer-Wagner S, Mayer W, Maegerlein S, Linke R, Jansson V, Muller PE. Use of 18F-FDG-PET in the diagnosis of endoprosthetic loosening of knee and hip implants. *Arch Orthop Trauma Surg* 2010 Oct; 130(10): 1231-1238.
- [25] Temmerman OP, Raijmakers PG, Berkhof J, Hoekstra OS, Teule GJ, Heyligers IC. Accuracy of diagnostic imaging techniques in the diagnosis of aseptic loosening of the femoral component of a hip prosthesis: A meta-analysis. *J Bone Joint Surg Br* 2005 Jun; 87(6): 781-785.
- [26] French TH, Russell N, Pillai A. The diagnostic accuracy of radionuclide arthrography for prosthetic loosening in hip and knee arthroplasty. *Biomed Res Int* 2013; 2013: 693436.