All the authors declare that there is no potential conflict of interest referring to this article.
keywords found in DeCS (Descriptors in Health Sciences) and MeSH (Medical Subject Headings): neoplasm seeding and biopsy with their counterparts in English and Spanish at all bases. In addition to these descriptors, we carried out a search with the following intersections of free terms, used because of their relevance to the topic studied: biopsy tract AND musculoskeletal tumors; biopsy tract AND musculoskeletal cancer; and biopsy tract AND musculoskeletal neoplasm, with their corresponding terms in English and Spanish on all databases. We were also consulted the references of selected articles for the search of relevant articles. All articles that addressed tumor contamination in the biopsy tract in musculoskeletal system were also included. Articles that addressed tumor contamination in the musculoskeletal system were also included. Articles that addressed tumor contamination in tract biopsy performed on systems other than the musculoskeletal, and articles that addressed contamination occurred in tumor sites other than the biopsy tract were excluded. Limits were used for articles in English, Spanish and Portuguese languages. No limits on publication date were used.

RESULTS

A total of 2,858 articles were retrieved, of which 2,684 were excluded by their title, since they were not adequate to the subject under study or by being duplicated in the databases, leaving 174 papers selected for summary reading. From reading the abstract, 35 articles were selected for full text reading. Of these 35 articles, only seven were selected by inclusion and exclusion criteria. Additional four articles not retrieved through the databases were also selected, but were found in the references of included articles and selected due to their relevance to the study. (Figure 1) Thus, 11 articles were selected to this systematic review. (Tables 1 and 2) Of the 11 articles, seven are case reports,16,19-24 (Table 1) and four articles are retrospective, cohort or prospective studies.13,17,18,25 (Table 2) For a better presentation of the results, the articles were divided into two tables. In Table 1 the variables presented are: author, year of publication, number of cases, age, gender, tumor site, type of tumor, biopsy technique, definition of contamination criteria, the time interval between biopsy and contamination diagnosis, and follow up. In Table 2 are presented the variables author, year of publication, number of cases in the sample, type of tumor, biopsy technique, chemotherapy applied, total sample contamination, contamination according to the biopsy technique, contamination according to chemotherapy and definition of contamination criteria.

DISCUSSION

The first thing to note is the low number of studies in the literature studying the contamination of the biopsy tract by tumor cells in the musculoskeletal system. The heterogeneity of articles does not allow the application of statistical analysis (meta-analysis). In an attempt to trace the profile of patients with contamination of the biopsy tract, it is observed that the case reports addressed 10 cases of contamination of the biopsy tract in the musculoskeletal system. For these cases, the age ranged from 72 to 74 years old.13 Eight male patients16,19-24 and two female patients19 have been reported. In cohort studies, it is observed that it is not possible to explore the epidemiological characteristics regarding to age and gender, since the authors report these data only for the overall group, not being possible to distinguish between patients who did show and those who showed no contamination of the biopsy tract. These observations reinforce what is perceived in the orthopedic oncology clinical practice, as the literature does not support the possibility of the variables gender or age to influence the occurrence of contamination in the biopsy tract. The perception that the biopsy tract may be contaminated seems to have been reinforced among the orthopedic community with the work of Cannon and Dyson15, who reported a statistically significant lower occurrence of local tumor recurrence where the biopsy tract performed by open technique was resected, compared with cases in which it was not resected. It is observed that in none of the 10 cases reported in the selected articles the biopsy tract had been resected. All cases evolved to local relapses.16,19-24 In articles on cohort studies, the work of Kaffenberg et al.18 and Saghieh et al.25 the biopsy tract was not removed in any of the patients studied, and there was no local tumor recurrence. In the works of Mohana et al.17 and Ribeiro et al.13 all biopsy tracts were removed, and presence or absence of local recurrence was not reported. However, in the work of Mohana et al.17 five of 26 patients (19.2%) were contaminated in the biopsy tract. On the other hand, in the work by Ribeiro et al.13 contamination occurred in 25 patients (32%). It is observed by analyzing the literature, that the possibility of local recurrence on unremoved biopsy tract is quite real, the practice of not resecting the biopsy tract appearing not at all safe, despite otherwise shown by Kaffenberg et al.18 and Saghieh et al.25.

Acta Ortop Bras. 2014;22(2):106-10
Some authors believe that the percutaneous biopsy technique, by involving less manipulation of tumor tissue, implies in a lower occurrence of contamination in the tract. When analyzing the studies surveyed for this systematic review, it is observed that of 10 reported cases, percutaneous biopsy was performed in seven, open in one case and in two others the biopsy technique was not informed. Regarding cohort studies, the work of Mohana et al. reported the occurrence of two cases of contamination in six open biopsies (33.3%) and three contaminations in 20 cases of percutaneous biopsy (15%). No reference was made to the criteria for choosing the biopsy technique, as it was not informed whether the two groups were homogenous. Although many authors believe that the percutaneous biopsy technique has a lower risk of contamination of its path when compared to the open technique, no statistical method was used to test this hypothesis.

### Table 1. Case reports of contamination of the biopsy tract of the musculoskeletal system according to the literature.

| Author/year Reference | Nº of cases | Age in years | Gender | Tumor location | Type of tumor | Biopsy technique | Criteria for definition of contamination | CT | ΔT | Follow up |
|-----------------------|-------------|--------------|--------|----------------|---------------|-----------------|------------------------------------------|-----|-----|----------|
| Citron et al., 1984   | 01          | 53           | M      | Lung           | Small cell lung carcinoma | Percutaneous | Histology of subcutaneous lesion in biopsy site | Yes | 14 months | Disseminated disease |
| Ginaldi e Williams, 1985 | 01          | 74           | M      | Lymphatic system | non-Hodgkin Lymphoma | Percutaneous | Histology of lesion in biopsy site | No | 11 months | Disseminated disease |
| Davies, et al., 1993  | 01          | 18           | M      | Femur distal   | Osteosarcoma | Percutaneous | Histology of nodular lesion in biopsy site | Yes | 18 months | Ni |
| Schwartz e Spengler, 1997 | 03          | 49           | F      | Pelvis         | Fibro sarcoma | Percutaneous | Tumor histology in the biopsy tract region | No | 37 months | Ni |
| Iemsawatdikul et al., 2005 | 01          | 7            | M      | Multifocal     | Osteosarcoma | Open | Histology of recurring tumor along the biopsy tract | No | Ni | Disseminated disease |
| Fowler, et al., 2008  | 02          | 48           | M      | Lymphatic system | Follicular Lymphoma | NI | Edema and pain in biopsy site. Biopsy revealed follicular lymphoma | No | 10 days | Death |
| Zoccali et al., 2009  | 01          | 47           | M      | L4             | Chondrosarcoma | Percutaneous | Infiltration in the tract detected by NMR | No | 1 month | Disseminated disease |

CT: Chemotherapy; Δt: time interval between biopsy and tract contamination diagnosis; NI: Not informed; M: Male; F: Female; NMR: Nuclear magnetic resonance; L2: second lumbar vertebra; L4: fourth lumbar vertebra; CT: computed tomography; CT: bone biopsy for staging performed. Underwent CT for treatment of small cell lung carcinoma. Underwent radiotherapy and CT for misdiagnosed metastatic carcinoma. Underwent radiotherapy and CT for misdiagnosed adenocarcinoma. Underwent CT for treatment of lymphoma. Patient had two biopsies, one before and one after CT, not being clear which one caused tract contamination.

### Table 2. Cohort studies regarding contamination of the biopsy tract of the musculoskeletal system according to the literature.

| Author/year Reference | Nº of cases | Type of tumor | Biopsy technique | Ct | Total contamination in sample | Contamination according to biopsy technique | Contamination according to ct | Criteria to define contamination |
|-----------------------|-------------|---------------|-----------------|----|-------------------------------|-------------------------------------------|-------------------------------|----------------------------------|
| Mohana et al., 2007   | 26          | Osteosarcoma  | Open 6          | Yes | 5/26 (19,2%)                  | Open 2/6 (33,3%)                         | Yes 3/24 (12,5%)               | Histological study of biopsy tract routinely removed during tumor resection |
| Ribeiro et al., 2009  | 25          | Bone and soft part tumors | Open 7 | No | 8/25 (32%)                   | Percutaneous 4/18 (22,2%)               | -                             | Histological study of biopsy tract routinely removed during tumor resection |
| Kaffenberg, Wakely Jr and Mayerson, 2010 | 20 | Bone and soft part tumors | Open 0 | Data not allow | 0 | Closed 0 | - | No local remission in non-removed biopsy tract |
| Saghiieh et al., 2010 | 10          | Osteosarcoma and Ewing’s Tumor | Open 0 | Yes | 0 | Open | Yes 0 | No local remission in non-removed biopsy tract |

CT: Neoadjuvant chemotherapy. NI: Not informed. Of five cases with contamination, two did not receive neoadjuvant CT due to large tumor extension. All bone tumors underwent percutaneous biopsy and all soft tissue tumors open biopsy by mini-incisions. Authors did not provide clear information about CT, just claim that 16 (80%) of 20 patients received adjuvant and/or neoadjuvant CT.
In the study by Ribeiro et al.,13 four contaminations occurred in seven open biopsies (57.1%) and four in 18 percutaneous (22.2%). The authors also did not perform statistical tests to assess the significance of these differences. It is emphasized that in this work bone tumors and soft tissue tumors were studied, and all bone tumors underwent percutaneous biopsy and all soft tissue tumors underwent open biopsy through mini incisions. Thus, comparing the incidence of contamination between open and percutaneous techniques in this study, it should be noted that the biopsy technique of choice was different for the different types of tumor, making two very heterogeneous groups. In the study of Kaffenberg et al.,18 and in Saghieh et al.,25 all biopsies were performed by percutaneous technique. In these two studies there has been no contamination in the biopsy tract. Although there is a perception that with the percutaneous technique the chance of contamination is lower, the heterogeneity between studies and the possibility of methodological flaws prevent an accurate conclusion. The main aspect shown in the literature is that tumor contamination in biopsy tract is real even in biopsies performed by percutaneous techniques, reinforcing the need for removal of the path during tumor resection.

Another issue raised in the literature is the influence of tumor type on the occurrence of tumor contamination in the biopsy tract.13,26 In the ten reported cases, there is a very wide variety in the types of tumors: two cases of osteosarcoma,13,26 one case of chondrosarcoma,26 one case of fibrosarcoma,19 one case of pleomorphic sarcoma,19 one case of chordoma,19 three cases of lymphoma22,24 and a case of small cell lung carcinoma.21 In these last four types, a bone biopsy for staging the primary tumor was performed. Regarding the cohort articles, Mohana et al.,17 studied osteosarcoma cases and found five contaminations (19.2%) in 26 cases. Moreover, the study of Saghieh et al.,25 in which 25 cases of osteosarcoma and Ewing’s sarcoma were analyzed, no contamination occurred. In the work of Kaffenberg et al.,18 who analyzed various soft tissue and bone tumors reported no contamination. Ribeiro et al.,13 who also studied bone and soft tissue tumors, found four contaminations (57.1%) in seven soft tissue tumors; and four contaminations (22.2%) in 18 bone tumors. The latter authors suggest that the greater cellularity and smaller amount of matrix, characteristics of soft tissue sarcomas, are related to greater cell spreading compared with bone tumors. It is noteworthy, however, that no statistical test was performed to evaluate the significance of this difference. From the foregoing, it is clear the uncertainty about the influence of the type of tumor on the occurrence of tumor contamination in the biopsy tract in the musculoskeletal system. The great heterogeneity among the studies does not allow a more detailed comparison.

Over the last decades, the treatment of tumors of the musculoskeletal system has been greatly influenced by adjuvant methods. Chemotherapy has been shown to be an effective method in the treatment of some bone tumors, particularly osteosarcoma and Ewing’s sarcoma, accounting for a historic change in the prognosis of these tumors, which became more favorable after the introduction of this therapeutic modality.14,27,28 The neoadjuvant chemotherapy administered before surgical resection of the tumor aims to induce tumor regression, allowing a surgical treatment with a lower functional impairment.27,29 and reduce tumor spread at surgery. Some authors believe that chemotherapy has a protective effect in the control of tumor infiltration in the biopsy site.17,18 On this issue, the first aspect to be considered is the time that chemotherapy would be administered to have a protective effect. The second issue is that not all tumor types benefit from this therapy. Thus, the study of this protective effect would be unique for tumors amenable to chemotherapy. Furthermore, the sensitivity to chemotherapy is a complex issue with wide variation in the response to each individual patient and for each chemotherapy approach.26-28,30

Another issue is that at different times studies used different chemotherapy protocols, also effectively different, making difficult the analysis and comparison between studies. By observing this effect of chemotherapy by evaluation of the work selected in this systematic review, we find it extremely difficult to extract the information from the articles. In the seven case reports, in general, the authors did not provide clear information on the administration of chemotherapy. In the 10 cases reported, chemotherapy was not administered in the period between biopsy and the contamination diagnosis in five patients.19,20,22-24 In two cases treatment chemotherapy for the primary tumor was done, being one case of osteosarcoma and one case of small cell lung carcinoma.21 In two other cases, chemotherapy was administered in order to treat a tumor which was misdiagnosed.19 Thus, given the imprecise efficacy of the chemotherapy protocol employed in these two cases it is impossible to conclude on the possible role of chemotherapy in protecting – or not – the tumor contamination. Finally, it is not possible to analyze the role of chemotherapy in one case reported by Fowler et al.24 because the patient underwent two biopsies, one before and one after chemotherapy treatment, being not clear in which of them tract contamination occurred. Thus, effectively, only two of the 10 cases reported could likely benefit from chemotherapy protective effect.16 In cohort studies, the paper from Ribeiro et al.13 does not report on the administration of chemotherapy or not, and data from Kaffenberg et al.18 does not allow any analysis, since the authors state that only 16 (80%) of 20 patients received adjuvant and/or neoadjuvant chemotherapy, without further details. Mohana et al.17 observed that the occurrence of tumor contamination in patients receiving neoadjuvant chemotherapy was 12.5% (three of 24 cases). In this study, the two only cases which did not receive neoadjuvant chemotherapy, due to their large tumors, presented with contamination on the biopsy tract. It is noteworthy, however, that the three patients who received neoadjuvant chemotherapy and presented contamination showed a poor response to chemotherapy. In the study of Saghieh et al.,25 in which neoadjuvant chemotherapy was given to all patients, there was no contamination in the biopsy tract. The studies reveal that although limitations may hinder the assessment of the protective effect of chemotherapy against tumor contamination, the observations of the outcomes of Mohana et al.17 and Saghieh et al.25 seem to reinforce the idea that this therapy modality exerts some protective effect against the occurrence of this complication, although other not controlled variables in these studies may jeopardize this conclusion.

Regarding the prognosis, of 10 cases reported five did not inform follow up.16,19,24 One patient died24 and four evolved with spreading of the disease.20,23 Of the cohort studies, the two
studies in which occurred contamination do not mention follow up. 13,17 Although cohort papers do not reinforce this hypothesis, not because they oppose to it, but they do not provide the information, the cases reported in the literature show a strong tendency to the belief that contamination the biopsy tract implies an unfavorable prognosis.

Regarding the criteria for defining contamination, it is observed that most authors used histopathology methods, 13,16,17,19,21-24 well recalled by Ribeiro et al., 13 when studying biopsy tracts by histopathology methods, a major issue is whether it is possible to pinpoint the location where the biopsy instrument has previously passed through. For this, the authors have suggested the use of local histology alterations, secondary to the aggression promoted by biopsy to the tissue as a marker of the site of biopsy histology. One aspect that deserves to be recalled is that none of the studies analyzed points out tumor staging as an important factor for contamination in the biopsy tract. Moreover, the range of variables that can interfere with presence or absence of contamination were not or could not be controlled in these studies, making difficult to draw further conclusions. Several points can be considered regarding the selected works, including the lack of studies with better methodological design. The difficulties seem to be related to the fact that the relativity of tumors of the musculoskeletal system and thus, the limitation of samples, the heterogeneity of these tumors and the large number of variables that may interfere with the contamination of biopsy tract by tumor cells. Certainly, these are issues that hinder studies with better methodologies, with standardization of unsatisfactory and variables control.

**FINAL CONSIDERATIONS**

The characteristics of tumor contamination in the biopsy tract in the musculoskeletal system are quite inaccurate according to the literature, although some questions may be raised:

- **Age and gender seem to have no influence on the occurrence of this complication;**
- **In the absence of resection in the biopsy tract, the possibility of local recurrence is quite real;**
- **It is uncertain the influence of the tumor type on the occurrence of contamination;**
- **It is not possible to conclude with certainty whether the percutaneous biopsy technique has a lower chance of contamination;**
- **It is likely that chemotherapy has a protective effect against tumor contamination in the biopsy tract;**
- **It is expected that patients presenting contamination along biopsy tract evolve with an unfavorable prognosis.**

**REFERENCES**

1. Chojniak R, Isberrner RK, Viana LM, Yu LS, Alta AA, Soares FA. Computed tomography guided biopsy needle: experience from 1,300 procedures. São Paulo Med J. 2006;124(1):10-4.
2. Siqueira KL, Viola DCM, Jesus-Garcia R, Gracitelli GC. Correlação do tipo de biópsia e sua validade diagnóstica nos tumores músculo-esqueléticos em distintas topografias. Rev Bras Ortop. 2008;43(1):27.
3. Enekeing W. The issue of the biopsy. J Bone Joint Surg Am. 1982;64(8):1119-20.
4. Enneking WF. The issue of the biopsy. J Bone Joint Surg Am. 1982;64(8):1119-20.
5. Ribeiro MB, Oliveira CRCM, Baptista AM. O papel da biópsia e sua validade diagnóstica nos tumores músculo-esqueléticos. Rev Bras Ortop. 1993;75(4):616-21.
6. Castone AE, Barbì-Grãoalves JC, Aguiar S. Eficácia da biópsia com agulha nos tumores ósseos. Rev Bras Ortop. 1996;31(11):89-14.
7. David A, Rios AR, Tarrago RP, Dalmína V. Biópsia com agulha nos tumores ósseos. Rev Bras Ortop. 1996;31(11):89-92.
8. Mankin HJ, Mankin CJ, Simon MA. The hazards of the biopsy. J Bone Joint Surg Am. 1979;61(3):137-40.
9. Markin HU, Lange TA, Scharier SS. The hazards of biopsy in patients with malignant bone and soft-tissue tumors. J Bone Joint Surg Am. 1982;64(8):1119-20.
10. Mankin HJ, Mankin CJ, Simon MA. The hazards of the biopsy. J Bone Joint Surg Am. 1982;64(8):1119-20.
11. Ribeiro MB, Oliveira CRCM, Baptista AM. O papel da biópsia percutânea na tomografia computadorizada. Rev Bras Ortop. 1999;34(1):77-80.
12. Skrzynski MC, Biermann JS, Montag A. Simon MA. Diagnostic accuracy and charge-savings of outpatient core needle biopsy compared with open biopsy of musculoskeletal tumors. J Bone Joint Surg Am. 1996;78(5):666-63.
13. Saghieh S, Masrouha KZ, Musallam KM, Mahfouz R, Abboud M, Khoury NJ, et al. Needle tract seeding after bone marrow biopsy. South Med J. 1985;78(8):1007-8.
14. Siqueira KL, Viola DCM, Jesus-Garcia R, Gracitelli GC. Correlação do tipo de biópsia e sua validade diagnóstica nos tumores músculo-esqueléticos em distintas topografias. Rev Bras Ortop. 2008;43(1):27.
15. Skrzynski MC, Biermann JS, Montag A. Simon MA. Diagnostic accuracy and charge-savings of outpatient core needle biopsy compared with open biopsy of musculoskeletal tumors. J Bone Joint Surg Am. 1996;78(5):666-63.
16. Enekeing W. The issue of the biopsy. J Bone Joint Surg Am. 1982;64(8):1119-20.
17. Ribeiro MB, Oliveira CRCM, Baptista AM. O papel da biópsia percutânea na tomografia computadorizada definitivo na suspeita de lesões cartilaginosas malignas do esqueleto. Rev Bras Ortop. 1999;34(1):77-80.
18. Skrzynski MC, Biermann JS, Montag A. Simon MA. Diagnostic accuracy and charge-savings of outpatient core needle biopsy compared with open biopsy of musculoskeletal tumors. J Bone Joint Surg Am. 1996;78(5):666-63.
19. Echebheria M, Camargo OP, Croci AT, Oliveira CRDM, Baptista AM. O papel da biópsia percutânea na tomografia computadorizada definitivo na suspeita de lesões cartilaginosas malignas do esqueleto. Rev Bras Ortop. 1999;34(1):77-80.
20. Skrzynski MC, Biermann JS, Montag A. Simon MA. Diagnostic accuracy and charge-savings of outpatient core needle biopsy compared with open biopsy of musculoskeletal tumors. J Bone Joint Surg Am. 1996;78(5):666-63.
21. Echebheria M, Camargo OP, Croci AT, Oliveira CRDM, Baptista AM. O papel da biópsia percutânea na tomografia computadorizada definitivo na suspeita de lesões cartilaginosas malignas do esqueleto. Rev Bras Ortop. 1999;34(1):77-80.
22. Ribeiro MB, Oliveira CRCM, Baptista AM, Caiero MT, Salzivan MS. Incidência de maligns in infiltração na biopsy tract de osteosarcoma. Malays Orthop J. 2007;1:7-10.
23. Kaffenberger BH, Wakely PE Jr, Mayerson JL. Local recurrence rate of fine-needle aspiration biopsy in primary high-grade sarcomas. J Surg Oncol. 2010;101(7):618-21.
24. Schwartz HS, Spengler DM. Needle tract recurrences after closed biopsy for sarcoma: three cases and review of the literature. Ann Surg Oncol. 1997;4(3):229-36.
25. Zocca C, Prencipe U, Erba F, Vidri A, Filippo F. Biopsy can determinate tumoral contamination: a case report of chondrosarcoma. Eur J Radiol Extra. 2009;72:79-81.
26. Citron ML, Krasnow SH, Grant C, Cohen MH. Tumor seeding associated with bone marrow aspiration and biopsy. Arch Intern Med. 1984;144(1):177.
27. Ginaldi S, Williams CD. Seeding of malignant lymphoma along the tract after bone marrow biopsy. South Med J. 1985;78(8):1007-8.
28. Imaeawatidkul K, Gooding CA, Tworrey EL, Kim GE, Goldsby RE, Cohen I, et al. Seeding of osteosarcoma in the biopsy tract of a patient with multifocal osteosarcoma. Pediatr Radiol. 2005;35(7):717-21.
29. Fowler N, Aslati E, Chenos B. Needle tract seeding after bone marrow biopsy in non-Hodgkin lymphoma. Leuk Lymphoma. 2006;49(1):156-8.
30. Saghieh S, Masrouha KZ, Musallam KM, Mahfouz R, Abboud M, Khoury NJ, et al. Needle tract seeding after bone marrow biopsy. South Med J. 1985;78(8):1007-8.