Percutaneous biopsy in oncological pathology of the spinal column

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Abstract

Background: Among oncological patients there is a group of patients with outcomes hard to predict because of few possibilities to diagnose, even though there are a lot of procedures, some of them being very painful. Absence of a diagnose lowers the chances of healing even before treatment starts, fact that makes patients refuse specific therapy. Often, these patients are referred to different medical centers during the short life that they have left. We are talking about patients in whom the clinical signs are metastasis; meanwhile the primary tumor doesn't have any manifestations at all. Percutaneous biopsy of the spinal column is a minimal invasive and rapid technique that obtains tissue samples from the vertebral body, intradiscal regions and paravertebral regions. Despite progress of computed tomography and magnetic resonance imaging technologies, basic diagnosis of different pathologies of the spinal column remains difficult. In most of the cases, a tissue sample is needed to settle a clear diagnosis. Percutaneous biopsy is preferred over the open biopsy because of the low costs, morbidity and mortality. The aim of this article is to review and to highlight in details the efficiency of percutaneous biopsy, by pointing out its influence on the treatment and decisions in such branches like surgery, chemotherapy, radiotherapy depending on the morphological nature of the lesions.

Conclusions: Percutaneous biopsy of the spinal column is the elective procedure in definitive diagnosis of pathological lesions.
Key words: percutaneous biopsy, metastasis, tumour, spine.

Introduction

Among oncological patients there is a group of patients with outcomes hard to predict because of few possibilities to diagnose, even though there are a lot of procedures, some of them being very painful. Absence of a diagnose lowers the chances of healing even before treatment starts, fact that makes patients refuse specific therapy. Often, these patients are referred to different medical centers during the short life that they have left. We are talking about patients in whom the clinical signs are metastasis; meanwhile the primary tumor doesn't have any manifestations at all [1].

Studies made on patients with metastasis without a known primary tumor, show that, until now, there is no optimal algorithm for diagnosing patients with metastasis with unknown primary tumor, an adequate determination of different methods of diagnosis and evaluation of metastasis does not exist [1].

Studies of autopsies with bone metastasis have 27% incidence in patients with carcinomas, 47-85% of whom die of breast cancer, 33-85% – of prostate cancer and 32-60% – of lung cancer. Bone metastasis may be the first clinical manifestation in almost 20% of patients with systemic cancer [57].

Global incidence of bone metastasis in patients with all kinds of cancer is about 70%. After lungs and liver, bones are on the 3rd place of metastasis. Out of all metastasis of the spinal column, 3% are primary unknown, and 75% derive from secondary tumors. About 30% of patients with cancer have metastasis at the moment of diagnose [63].

Metastases appear in a way that does not follow the laws of typical dissemination of tumors with known localization [1]. D. A. Casciato [25] compared the group of patients with metastasis with unknown primary tumor (later the primary tumor was found), with the group of patients with unknown source of the primary tumor and discovered the following particularities: patients with lung cancer had bone metastasis in 30-50% of the cases, and patients that had metastasis with an unknown focus (which later was found in the lungs), had bone metastasis only in 5% of the cases. In a similar way, bone metastases were found in 5-10% of patients with pancreatic cancer, and patients with metastasis with an unknown focus (which was later found in the pancreas) represented 30% of the cases. Metastases in the lungs and liver are found in 15% of patients with prostate cancer; meanwhile patients with metastasis with unknown focus (later discovered in the prostate), represent 50% of the cases of lung and liver metastasis. Atypical dissemination of tumors prevents essentially the process of identification of the primary focus, which in most of the cases complicates the localization's prognosis (according to the identified metastasis) [25].

It was established that during a thorough examination, that includes all methods of diagnosis, the primary focus could be identified in only 7.1% of the patients [43, 66]. Costs of examination of such a patient in USA are about 18.000 USD. The mean life expectancy of these patients does not exceed 8.1 months [62, 68].

Choosing a correct treatment tactics for spinal metastasis is difficult and depends on many factors, primary the life expectancy and the balance between the surgery risks against the risk of quality of life improvement. Prognosis was designed to help the clinician to decide the optimal tactics, but until now, we are against the version of choosing the best option, that in most of the cases is based on the subjective experience of the surgeon as well [22]. Generally, it is admitted that a surgery is indicated when a patient has a life expectancy more than 3 months [53].

Out of all oncologic patients without apparent clinical metastasis, only 50% can be cured with loco-regional treatments (surgery, radio-surgery), and according to recent data, about 60% of patients have microscopic metastasis at the moment of diagnosis. Metastases are responsible for almost 90% of deaths from cancer. About 5-30% of patients with metastasis in the spinal column have neurological symptoms. Metastasis

represents the fundamental process that differentiates the benign and malignant tumors, that transforms an organ cancer in a disease of the entire body, systemic disease [22, 52], and these patients become patients of a multi-modal branch [12, 31, 58, 59, 146]. Prognosis for patients with metastasis in the spinal column is the most important factor in choosing the correct tactics of treatment [16, 26].

The key to success in deciding the tactics of treatment of tumors of the spinal column is the histological type of the tumor. Tissue biopsy represents the basis of oncology.

Biopsy can be of three types:

- Percutaneous (transpedicular, transfacetar, lateral approaches);
- Open incision (when a larger quantity of tissue is required);
- Excisional.

Before imagistic guidance techniques of spinal column biopsy were developed, open biopsy procedure was necessary for definitive diagnosis. The advantage of open biopsy was double: the first was direct visualization, big and multiple tissue samples can be obtained for histological examination; and the second was the possibility of spine surgical decompression and / or column stabilization.

Percutaneous biopsy of the spinal column was firstly described by Minge in 1934 and then by Robertson and Ball in 1935 [56]. Though, their procedure did not use imagistic guidance. Siffert and Arkin [60] used posterior-lateral approach for spinal biopsy with radiographic guidance. Biopsy with imagistic guidance was reported in literature in 1949 with conventional radiography, followed by fluoroscopy in 1969, computed tomography (CT) in 1981, magnetic resonance imaging (MRI) in 1986, and CT fluoroscopy in 1996 [56]. At the beginning, open biopsies were performed, but percutaneous biopsy proved to be a more rapid, cost effective method with less complications [2, 3, 6, 17, 54].

There are 5 major indications for percutaneous biopsy of spinal lesions:

1. In order to identify an unknown lesion before a treatment plan is established;
2. Lesion that does not respond to empirical conventional treatment;
3. Infection that does not respond to 6-week treatment;
4. Fracture from compression on an unknown focus;
5. Intensification or persistence of pain in a patient with history of Paget disease [46].

Additional indications are:

- Metastasis confirmation in case of known primary focus;
- Diagnosis of primary bone lesion;
- Specific of nonspecific infection, with antibiotic sensibility;
- Determination of chemotherapy efficiency;
- Multiple myeloma cytological diagnosis;
- Benign lesion confirmation (osteoporosis, renal dystrophy);
- Diagnosis confirmation through histology and immunehistochemical methods in cases of FFD tumors;
- Symptomatic synovial cysts.

The major indication of this method is the correct choice of subsequent management of oncological patients, important in case of multimodal treatment's tactic change in this category of patients [4].

Among the first indications for biopsy are the lithic or blastic lesions, soft expansive process in the spinal column in patients with oncological history [5, 6, 61].

The second place after metastasis are discitis, with adequate planning of management of the symptomatic treatment, surgical radicalness, prevention of infection progress to sepsis, of local progression of the infection in cases of metallic implants [6, 7, 8], followed by pathological fractures, aspiration of symptomatic synovial cyst, etc [6, 9, 10].

Relative contraindications are:

- Hemorrhagic diathesis, coagulopathies, thrombocytopenia (50.000);
- Infection, including infection at the level of projection of the biopsy, including adjacent infection of the affected vertebrae;
- Non-accessible localization, for example C1 arch, the tooth of C2, bone fusion;
- Uncritical patient, with the need of general anesthesia;
- Pregnancy;
- Allergy to medications required for the procedure;
- Patients with medullar compressions at the level of interest [10, 11].

An absolute contraindication for percutaneous biopsy is coagulopathy. Nevertheless, even this condition, if correctly managed in advance, can be sufficiently corrected in order to permit the surgeon to make the procedure. If a vascular tumor, such as renal metastasis, is suspected, angiography should be taken into consideration in preliminary diagnostics.

Imagistic methods of intra-operatory guidance are:

Ultrasonography. Offers real time monitoring, it is rapid, cheap, avoids radiation and offers the possibility to visualize the tip of the needle during the entire procedure. It is often used in diagnostics of parenchymal organs such as: liver, thyroid gland, pancreas, lungs, prostate, breast. Its applicability at the level of spinal column resumes to superficial lesions of cervical spine [12, 13].

Fluoroscopy. The first fluoroscopic procedure was made in 1949, followed by single plan, bi-plan and C-arm fluoroscopy [14, 15].

Studies about fluoroscopic guidance and CT uncover the advantages and disadvantages of each procedure [46, 54, 56, 65].

Computed tomography (CT) has been used more than 20 years. It is a standard for many institutions. CT offers an exact trajectory planning, avoids lung passage at the thoracic level or other vital organs, it also offers to delimitate solid, necrotic, sclerotic lesions and exact depth. The disadvantage is the duration of the procedure and the dose of radiation for the patients and medical staff, and cost as well [18, 19].

CT fluoroscopy was described for the first time in 1994 [19, 21], it combines the advantages of conventional fluoroscopy with real-time visualization of six concomitant images. CTF is useful for visualization of retro-peritoneal organs that

are prone to physiological movements. One of the major concerns about CTF is the great dose of radiation. Conventional fluoroscopy doses are measured in centigrays per minute of exposure, meanwhile, the doses of CTF are measured in centigrays per second of exposure [19, 21].

Magnetic resonance imaging is a unique method, but with many economical disadvantages, described in literature being 15% more expensive than other methods [23, 24]. First of all, the procedure is expensive, the instruments must be made of titanium, the duration of the procedure is increased, also patients must not have contraindications for this type of procedure [23].

Before the procedure, patients must be fully examined clinically and paraclinically as for a surgical intervention: complaints, history, oncological history, and contact with contagious diseases. If the patient takes aspirin or other NSAI drugs, they must be suspended 3 days prior the procedure, with renewal after the procedure; in case of infection suspect, suspention of antibiotics 48h prior the procedure, special attention is paid to anesthetics drugs [25, 27, 29].

The procedure is made in the operating room, under sterile conditions, or in an angiographic laboratory, with a specialized table, that allows C-arm rotations for rapid anterior and profile images. The positioning of the patient on the table depends on the affected region, for superior cervical region with trans-oral and oropharyngeal approach the position is dorsal, in the rest of the cases, the position is ventral. Indications for posterolateral or transpedicular approach depend on the localization of the lesion. If the lesion is located primarily in the intervertebral space, or in cases of infectious diseases, posterolateral approach is to be used. This approach is mandatory in cases of lesions in the inferior part of the vertebral body. However, if the lesion is situated in the posterior part of the vertebral body, or if the pedicle is implied, transpedicular method is very efficient for biopsy [55, 64]. In cases of lesions of the entire vertebral body, transpedicular approach is usually preferred [10. 36, 45, 50, 54].

Skin is treated in a standard way, 3 times, with antiseptics. The marking of the entrance point is made with the C-arm (necessary angle inclusive, which can be estimated based on CT). Skin incision is about 2-3mm, with local anesthesia made with 1% lidocaine infiltration through the pedicle. Under fluoroscopic guidance advancing through the pedicle is made in case of transpedicular approach, or lateralized in case of costotransverse approach. Biopsy material is taken from several superficial and profound regions, soft paravertebral tissue inclusive, if required, aspirational liquid is taken for cytologic, bacteriologic exam [30].

Taken material is being taken for necessary examinations: histological, cytological, immune histological or bacteriological if required. Schematically surgical approaches (fig. 1).

Histology is the tissue examination sampled from the patient. Cyto-pathology is the cell study obtained from the tissue by means of fine needle biopsy. Benign and malignant tumors have two basic components:

1. Neoplastic and proliferative cells – their parenchyma;
2. Supporting stroma made of connective tissue and blood vessels.

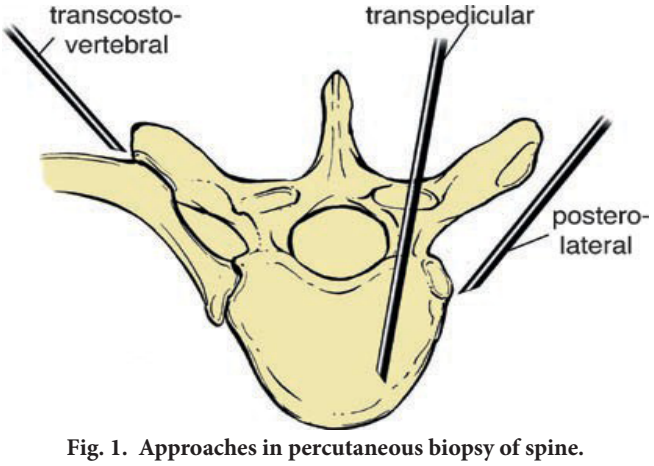

Fig. 1. Approaches in percutaneous biopsy of spine.

The parenchyma is the proliferative compartment of tumors and as a result determines the pathological compartment, tumoral growth and evolution that critically depends on its stroma [52].

Hyperplasia represents the physiological excessive proliferation of cells (pregnancy, breast-feeding, physical effort), compensatory proliferation (wounds, bone fractures, healing processes) and pathological (if the excess goes beyond the physical capacities). Tumoral growth doesn't obey any of these rules, neoplastic modifications can occur in hyperplastic tissues.

Dysplasia is a size, shape and cell organization disturbance in a tissue, as a result of growth and differentiation disruption caused by irritative factors, inflammation and hormonal factors/

Dysplasia is abnormal, but does not equal to malignancy [52].

Differentiation is about the functional and morphological features neoplastic cells resemble the normal cells; the absence of differentiation is called anaplasia [52].

Absence of differentiation or anaplasia is marked by a number of morphological modifications:

- Pleomorphic;
- Altered nuclear;
- Mitosis [28, 52].

There are national guidelines and standard protocols for pathological analysis of the majority of tumors. A vast number of staining can be made besides the standard staining with hematoxylin-eosine. Important progress of the techniques made it possible to offer results in an hour or one day. Immune histochemistry and molecular pathology are used in order to classify tumors [52].

The goal of immune histochemistry is to detect cellular or tissue-specific antigens by means of marked antibodies that can be visualized through microscopy of fluorescence. Immune histochemistry is very important in stabilizing the differentiation line in poorly differentiated tumors. The majority of pathologists use an approach based on steps. On the first step, they use generic markers that contain cytokeratins (for epithelial differentiation), melanocytic markers, CD 45 (leucocyte common marker, for hematopoietic differentiation) and vimentine (for mesenchymal differentiation). On the

second step, attention is paid to specific antibodies selected based on previous results [52].

Advantages of cytopathology:

- Small tissue lesions;
- Lesions that are not accessible for large biopsy;
- Patients' comfort;
- Rapid diagnosis.

Disadvantages of cytopathology:

- Limited possibility of detailed classification;
- Not capable to differentiate cancer.

Criteria that confirm diagnosis or at least suspect the diagnosis are:

1. Morphology of the cancer cell is different (size, shape) compared to the normal cell.
2. The nucleus of the cancer cell is bigger and is hyperchromatic than the normal cell, nuclei-cytoplasm ratio is bigger, nucleoluses are larger.
3. The number of cells in mitosis is greater in cancer cells, more than 20 mitosis per 1000 cells (1 in 1000 cells).
4. Abnormal mitosis, "giant cells", with polymorph features or multiple nuclei.
5. Normal tissue invasion of a neoplasm with high possibilities of metastasis [20].

Some authors claim that biopsy tissue with intra-operatory cytology had 96.9% sensibility, 100% specificity, 100% positive predictive value, negative predictive value of 87.5% well-correlated with the histological examination with 95.7% precision. The mean needed for result declaration was 8.9 +/- 1.7 minutes [38].

Complications in case of percutaneous biopsy of the spinal column are estimated to be less than 1% [31, 32].

Complications associated with percutaneous biopsy of the spinal column are:

1. Active bleeding;
2. Hematoma;
3. Vascular lesion;
4. Dural or radicular lesions (of the spine or nerves) with transitory or permanent neurological deficit.
5. Pneumothorax;
6. Infection, meningitis inclusive.

Most of the complications occur in the thoracic part of the spinal column: pleura / lung lesions, lesions of main vessels [33, 34], pneumothorax, radicular or medullar lesions with transitory neurologic deficit. Allergic reactions, even anaphylactic shock, are possible [35]. Post-procedure pain usually recedes after 24h. Hemorrhagic and infectious complications occur rarely.

Percutaneous biopsy of the spinal column is a well-known, efficient, rapid and less invasive technique that obtains tissue samples from the vertebral body, intradiscal regions and paravertebral regions [6, 10, 21, 24, 30, 36]. Despite progresses of CT and MRI technologies, basic diagnosis of different pathologies of the spinal column remains difficult. In most of the cases, a tissue sample is needed to settle a clear diagnosis. Percutaneous biopsy is preferred over the open biopsy because of the low costs, morbidity and mortality [6].

Efficiency of percutaneous biopsy in the management of spinal lesions was largely evaluated [10, 67]. The risk implied in percutaneous biopsy was estimated differently: 0% [44]. 2.2% [55], 7.6% [10] and 26% [29]. The most frequent complications reported were pulmonary, neurological and infectious complications. Precision of vertebral biopsy with posterolateral approach ranged between 50% and 90% [10, 29, 44, 45, 55, 67]. Other authors claim that the precision rate of percutaneous biopsy is 87-95%, and complications' rate is 0.2% [54].

Biopsy results which affect subsequent clinical management of the patient and will influence the treatment and decisions in such branches as surgery, chemotherapy, radiotherapy, antibiotic therapy depending on the morphological nature of the lesions.

Patients' survival with metastasis in the spinal column according to the morphology of the primary focus of the tumor (tab. 1).

Table 1

Patients' survival with metastasis in the spinal column

Type of cancer	Mean survival	5 years %	Mentions
Breast cancer	1-2 months	13%	
Prostate cancer	1-2 months	17%	
Lung cancer	3 months	2%	
Multiple mieloma	2-3 years		
Colo-rectal cancer	13 months		
Cervical cancer			The majority die in 18 months
Kidney cancer	1 year	30% if there is a single bone tumor	

Precision of percutaneous biopsy with different imagistic guidance methods is estimated in literature to be 88-100% [1, 37, 39, 40].

Positive prediction value of this procedure is 82%, negative prediction value is 100% [41]. Precision rate is higher in cases of metastasis or recurrent sarcoma, being 94% [41, 42, 44, 45, 47]. Capacity of culturing in cases of infection is low, ranging from 46% to 91% [48, 49, 50].

Conclusions

Percutaneous biopsy of the spinal column is a safe procedure, efficient and cost effective. It is the elective procedure in definitive diagnosis of pathological lesions of the spinal column.

References

1. Mereuță Ion. Tumorile maligne secundare cu focare primare necunoscute [Secondary malign tumors with unknown origin]. Chisinau, 2012;130.
2. Abbruzzese JL, et al. The biology of unknown primary tumors. *Semin. Oncolog.* 1993;20:238.
3. Abbruzzese JL, Abbruzzese MC, Hess KR, et al. Unknown primary carcinoma: natural history and prognostic factors in 657 consecutive patients. *J clin Oncolog.* 1994;12(6):1272-80.
4. Abrahm JL, Banfly MB, Harris MB. Spinal cord compression in patients with advanced metastatic cancer:„all I care about is walking and living my life„. *JAMA*. 2008;299:937-946.

5. Appel NB, Gilula LA. "Bull's-eye" modification for transpedicular biopsy and vertebroplasty. *Am J Roentgenol*. 2001;177:1387-9.
6. Ashizawa R, Ohtsuka K, Kamimura M. Percutaneous transpedicular biopsy of thoracic and lumbar vertebrae - method and diagnostic validity. *Surg Neurol*. 1999;52:545-51.
7. Avva R, Vanhemert RL, Barlogie B, et al. CT-guided biopsy of focal lesions in patients with multiple myeloma may reveal new and more aggressive cytogenetic abnormalities. *Am J Neuroradiol.* 2001;22:781-5.
8. Ball RP. Needle (aspiration) biopsy. *J Tenn Med Assoc*. 1934;27:203-6.
9. Bartels RH, Van Der Linclm YM, Van dr Groaf WT. Spinal extradural metastasis:review of current treatment options. *CA Cancer J Clin*. 2008;58:245-59.
10. Bender CE, Berquist TH, Wold LE. Imaging-assisted percutaneous biopsy of the thoracic spine. *Mayo Clin Proc*. 1986;61:942-950
11. Biopsy of the thoracic spine. *Mayo Clin Proc*. 1986;61:942-950.
12. Bradley W, Jacobs MD, et al. Evaluation and treatement of spinal metastasis: an overview. *Neurosurg. Focus*. 2001;11(6).
13. Buyukbebeci O, Karakurum G, Tutar E, et al. Biopsy of vertebral tumour metastasis for diagnosing unknown primaries. *J Orthop Surg*. 2010;18(3):361-3.
14. Carbone M, Barbanti M, Brodano G. Viral carcinogenesis. In Chang AE et al. Oncology – an evidence-based approach. New York: Springer, 2006;214-232.
15. Chew FS, Kline MJ. Diagnostic yield of CT-guided percutaneous aspiration procedures in suspected spontaneous infectious diskitis. *Radiology*. 2001;218:211-4.
16. Choi D, Crockard A, Bunger C, et al. Review of metastatic spine tumour classification and indications for surgery : the consensus statement of the Global Spine Tumour Study Group. *Eur Spine J*. 2010;19:215-222.
17. Chong-Suh Lee, Chul-Hee Jung. Metastatic Spinal Tumor. *Asian Spine J*. 2012;6(1):71-87
18. Coleman RE. Metastatic bone disease: clinical feature, pathophysiology and treatment strategies. *Cancer Treatment Rev*. 2001;27:165-76.
19. Czervionke LF, Fenton DS. Percutaneous spine biopsy. In: Fenton DS, Czervionke LF, editors. Image-guided spine intervention. Philadelphia: Saunders, 2003;141-87.
20. Daniel K, Steven Resnick, Garfin R. Vertebroplasty and Kyphoplasty, 2005;8.
21. Dave BR, Nanda A, Anandjiwala JV. Transpedicular percutaneous biopsy of vertebral body lesions: a series of 71 cases. *Spinal Cord*. 2009;47:384-9.
22. Choi D, Crockard A, Bunger C, et al. Review of metastatic spine tumour classification and indications for surgery: the consensus statement of the Global Spine Tumour Study Group. *Eur Spine J*. 2010;19(2):215-222.
23. Davis TM. Spinal biopsy techniques. In: Mcgraw JK, editor. Interventional radiology of the spine. Totowa: NJ: Humana Press Inc, 2004;181-96.
24. De Lucas EM, Mandly AG, Gutierrez A, et al. CT-guided fine-needle aspiration in vertebral osteomyelitis: true usefulness of a common practice. *Clin Rheumatol*. 2009;28:315-20.
25. Dennis A, Casciato DA, Barry B. Manual of clinical Oncology. Spiral-bound January 15, 1995, 3th edition.
26. Derek GJu, Yurter Al, et al. Diagnosis and surgical management of breast cancer metastatic to the spine. *WJCO*. 2014;5(3):263-271.
27. Dupuy DE, Rosenberg AE, Punyaratabandhu T. Accuracy of CT-guided needle biopsy of musculoskeletal neoplasms. *Am J Roentgenol*. 1998;171:759-62.
28. Frederick L Greene, David L. Cancer Staging handbook, 6th edition. New York: Springer-Verlag, 2002;1-26.
29. Fyfe I, Henry APJ, Mulholland RC. Closed vertebral biopsy. *J Bone Joint Surg*. 1983;65:140-143.
30. Garces J, Hidalgo G. Lateral Access for CT-guided percutaneous biopsy of the lumbar spine. *AJR*. 2000;174:425-26.
31. Gasbarrini A, Beisse R, Fisher C, et al. Spine metastasis. *Int J Surg Oncol*. 2011;375097.
32. Gerszten PC, Welch WC. Current surgical management of metastatic spinal disease. *Oncology*. 2000;14:1013-24.
33. Ghelman B. Biopsies of the musculoskeletal system. *Radiol Clin North Am*. 1998;36:567-80.
34. Gupta RK, Cheung YK, Al Ansari AG, et al. Diagnostic value of image-guided needle aspiration cytology in the assessment of vertebral and intervertebral lesions. *Diagn Cytopathol*. 2002;27:191-6.
35. Hadjipavlou AG, Kontakis GM, Gaitanis JN, et al. Effectiveness and pitfalls of percutaneous transpedicle biopsy of the spine. *Clin Orthop*. 2003;411:54-60.
36. Işik HS, Çagli S, Zileli M. Percutaneous Biopsy of the Spine: Analysis of 84 Cases. *Journal of Neurological Sciences (Turkish)*. 2012;29(2):258-265
37. Hecht S. Etiology of cancer: Tabaco. In: De Vita, Lawrence T.S., Rosenberg S.A., De Pinho R.A., Weinberg RA (eds): De Vita, Hellman, and Rosenberg's Cancer principles and practice of oncology 8th edition, Wolter Kluwer. Philadelphia: Lippincott Williams and Wilkins, 2008;147-244.
38. Naresh-Babu J, Neelima G, Reshma-Begum S.K. Increasing the specimen adequacy of transpedicular vertebral body biopsies. Role of intraoperative scrape cytology, January 27, 2014.
39. Jelinek JS, Kransdorf MJ, Gray R, et al. Percutaneous transpedicular biopsy of vertebral body lesions. *Spine*. 1996;21:2035-40.
40. Kang M, Gupta S, Khandelwal N, et al. CT-guided fine-needle aspiration biopsy of spinal lesions. *Acta Radiol*. 1999;40:474-8.
41. Kattapuram SV, Rosenthal DI. Percutaneous biopsy of skeletal lesions. *Am J Roentgenol.* 1991;157:935-42.
42. Klimo PJr, Schmidt MH. Surgical management of spinal metastasis. *Oncologist*. 2004;9:188-196.
43. Kollmann D, Hoetzenecker K, Prosch H, et al, Removal of a large cement embolus from the right pulmonary artery 4 years after kyphoplasty:consideration of thrombogenicity. *J Thorac. Cardiovasc. Surg*. 2012;143:122-124.
44. Laredo JD, Bard M. Thoracic spine: percutaneous trephine biopsy. *Radiology* 1986;160:485-489
45. Pierot L, Boulin A. Percutaneous Biopsy of the Thoracic and Lumbar Spine: Transpedicular Approach under Fluoroscopic Guidance. *AJNR Am J Neuroradiol*. 1999;20:23-25.
46. Lee CS, Jung CH. Metastatic spinal tumor. *Asian Spine J*. 2012;6(1):71-87
47. Leffler SG, Chew FS. CT-guided percutaneous biopsy of sclerotic bone lesions; diagnostic yield and accuracy. *Am J Roentgenol*. 1999;172:1389-92.
48. Lis E, Bilsky MH, Pisinski L, et al. Percutaneous CT-guided biopsy of osseous lesion of the spine in patients with known or suspected malignancy. *Am J Neuroradiol*. 1994;25:1583-8.
49. Logan PM, Connell DG, O'Connell JX, et al. Image-guided percutaneous biopsy of musculoskeletal tumors: an algorithm for selection of specific biopsy techniques. *Am J Roentgenol*. 1986;166:137-41.
50. Loredo JD, Bard M. Thoracic spine: Percutaneous trephine biopsy. *Radiology*. 1986;160:485-89.
51. Mackillop WJ, Dixon P, O·Sullivan B. The role of cancer staging in evidence-based medicine. In: Pollock R.E.(ed) UICC- Manual of clinical Oncology. 8th edition. New York: Willey-Liss, 2008:215-223.
52. Nagy V. Principii de oncologie generală. Cluj-Napoca, 2007;37-47.
53. National collaborating Centre for Cancer 2008. Metastatic spinal cord compression. Diagnosis and management of adults at risk of and with metastatic spinal cord compression. Nice Guidelines CG 75, TJ International Ltd, Cardiff, UK.
54. Pierot L, Boulin A. Percutaneous biopsy of the thoracic and lumbar spine: transpedicular approach under fluoroscopic guidance. *Am J Neuroradiol*. 1999;20:23-5.
55. Renfrew DL, Whitten CG, Wiese JA, et al. CT- guided percutaneous transpedicular biopsy of the spine. *Radiology*. 1999;180:574-576.
56. Robertson RC, Ball RP. Destructive spine lesions: diagnosis by needle biopsy. *J Bone Joint Surg (AM)*. 1935;57:749-58.
57. Schiff D, O·Neill BP, Suman VJ. Spinal epidural metastasis as the initial manifestation of malignancy: clinical features and diagnosis approach. *Neuroradiology*. 1997;49:452-56.
58. Sciubba DM., Gakaslan ZL. Diagnosis and management of metastatic spine disease. *Surg. Oncolog*. 2006;15:141-151.
59. Sciubba DM, Petteys RJ, Dekutoski MB, et al. Diagnosis and management of metastatic spine disease. *J Neurosurgery Spine*. 2010;13:94-108.
60. Siffert RS, Arkin AM. Trephine bone biopsy with special reference to the lumbar vertebral bodies. *J Bone joint Surg (AM)*. 1949;31:146-9.

61. Smith RA, Cokkinides V, Eyre HJ. Cancer screening in the United States, 2007: a review of current guidelines, practices, and prospects. *CA Cancer J Clin*. 2007;57:90-104.
62. Smith RA, Cokkinides V, Eyre HJ. Cancer screening in the United States, 2007: a review of current guidelines, practices, and prospects. *CA Cancer J Clin*. 2007;57:90-104.
63. Stylianidou S, Tzitzikas I, Chatzigiannaki A, et al. The current role of radiotherapy is vertebral hemangiomas without neurological signs. A case report and a review of literature. *Aristotle University Medical Journal*. 2013;40(1).
64. Sucu HK, Bezircioğlu H, Çiçek C, et al. Computerized tomography-guided percutaneous transforaminodiscal biopsy sampling of vertebral body lesions. *J Neurosurg*. 2003;99:51-5.
65. Tehranzadeh J, Browning CA. Percutaneous needle biopsy of the spine. *Acta Radiolog*. 2007;48(8):860-8.
66. Tourtienr JP, Cottez S. Images in clinical medicine. Pulmonary cement embolism after vertebroplasty. *J. Med.* 2012;366:258.
67. Babu VN, Titus VTK, Chittaranjan S, et al. Computed tomographically guided biopsy of the spine. *Spine*. 1994;19:2436-42
68. Zozulya YZ. Spinal cord and vertebral tumors. 2012. ISBN 978-966-460-016-0:400.00