Long-term experience with percutaneous biopsies of pelvic lesions using CT guidance

Petr Hoffmann, Michal Balik, Martina Hoffmannova, Jiri Spacek, Jiri Vanasek, Adam Rezac and Petr Dvorak

1Department of Radiology, Charles University Faculty of Medicine and University Hospital, Hradec Kralove, Czech Republic
2Department of Urology, Charles University Faculty of Medicine and University Hospital, Hradec Kralove, Czech Republic
3Faculty of Education, University of Hradec Kralove, Hradec Kralove, Czech Republic
4Department of Gynecology and Obstetrics, Charles University Faculty of Medicine and University Hospital, Hradec Kralove, Czech Republic

Abstract
To evaluate the accuracy, efficiency, complication rate, technical features, and relations among followed parameters of CT-guided percutaneous biopsies of the pelvic lesions. 140 biopsies in 136 patients for tumors, sizes 17–160 mm in largest diameter, were carried out in patients with probable tumorous pelvic process within ten years period. The patients were women in 77 cases and men in 59 cases, aged 21 to 87 years. The lesions size varied from 17 mm to 160 mm in largest diameter. In 135 biopsies (96.4%) results were true positive or true negative; only 5 procedures (3.6%) were histologically false negative and had to be verified surgically. Metastatic affection was the most common diagnosis (26.4%). Lymphomas were diagnosed in 25%; serous adenocarcinoma of ovary or uterine tube was verified in 15.7% of cases. Totally 7 complications (5%) were confirmed, all were minor hemorrhages. A statistically significant relation between the complication rate and hypervascular character (p = 0.00004), and between needle gauge and histological accuracy (p = 0.00429) was revealed. Core needle biopsy using percutaneous approach and CT guidance had a high overall accuracy in determining the final histological diagnosis including subtyping. Concurrently, the complication incidence was low.

Corresponding author:
Petr Hoffmann, Department of Radiology, Charles University, Faculty of Medicine and University Hospital, Hradec Kralove, Sokolska 581, 500 05, Czech Republic.
Email: petr.hoffmann@fnhk.cz
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Introduction
The pelvic cavity constitutes the anatomically complex inferior part of the body in direct connection with the abdominal space, varying in men and women. The pelvis is bounded by bony and muscle structures. In normal conditions, it contains connective tissue with nervous and lymphatic structures around iliac arteries, veins, and their branches. The visceral content forms the rectum (many times also parts of the small bowel), urinary bladder with distal ureters; in females, ovaries, fallopian tubes, uterus, vagina, and female urethra; in males, prostate, male urethra, seminal vesicles, ejaculatory ducts, and ducti deferentes.1

The spectrum of possible impairments is broad. Primary pelvic tumors are both a heterogenous and very common group of variable biological potential. Rectal carcinoma, prostate carcinoma, and gynecological tumors including cervix carcinoma belong in general among the most commonly diagnosed malignancies. Furthermore, many rare tumors from muscle or fibrous tissue, fat, peripheral nerve or nerve sheath, vessels, and germinal cell origin can be verified in the pelvis.2 Lymphomas form a specific category with frequent pelvic affection. Metastatic disease to the lymphatic nodes is an inseparable part of TNM classification.3 Also, some benign processes have tumor-like manifestations and also imaging morphological features.4 It is essential to acquire a relevant tissue specimen of these affections for the establishment of a final diagnosis and planning of further therapies.5

The pelvis is a region of several medical specialties. The rectum is the domain of surgery and gastroenterology; the urinary bladder and prostate pertain to urology, and female-specific diseases are the sphere of gynecology. All mentioned specialties use their own approaches and instruments for establishing diagnoses.6–8 Minimally invasive diagnostic methods using different image guidance have been preferred within the last decades over surgical excision biopsies. Computed tomography (CT) guidance was historically frequently used.9 More recently, ultrasonography has emerged as a more suitable technique due to the absence of ionizing radiation and the development of endoluminal instruments with a real-time procedure control possibility.10 On the other hand, several indications remain for establishing a diagnosis and using CT guidance. That is why we want to present our long-term results, verify the usefulness of this diagnostic approach and highlight important features of the procedure.

Materials and methods
Over the course of ten years, from February 2009 to February 2019, a group of 136 patients was retrospectively evaluated. Indication for the biopsy was established on the basis of clinical and imaging examinations; in the first step, ultrasonography (transabdominal or endoluminal) was commonly used. However, in all presented cases the
suspicion was verified by contrast medium enhanced computed tomography (CT), 18F-fluoro-2-deoxyglucose (18F-FDG) marked positron emission tomography/computed tomography (PET/CT) or magnetic resonance (MR). CT guidance was used after non-diagnostic attempts from other medical pelvic specialties.

Monitored parameters were age, gender, the lesions largest diameter, biopsy needle gauge, skin to process distance, number of samplings, mass vascularization, previous tumorous diseases in the patient's medical history, complications and their managing, final histological diagnosis including subtyping, and correlations with the results of appropriate therapies. Skeletal pelvic impairments and appropriate interventions were not included in the study.

The biopsies were performed in different anatomical pelvic parts. The patient’s position on the CT table – supine, side or prone - was selected on the basis of preprocedural imaging examinations. All of the presented interventions were carried out using CT guidance. The device Siemens Somatom Definition AS Plus (Siemens, Forchheim, Germany) was used.

Fully informed consent was obtained in all cases with an explanation of the procedure course and principles, the resulting consequences, possible complications, and their eventual solutions. All the patients were indicated by the multidisciplinary council (radiologist, gynecologist, oncologist or urologist). This study was approved by the institutional ethics review committee.

All biopsies were carried out using local anesthesia (Trimecaine, Zentiva, Prague, Czech Republic); neither conscious sedation nor general anesthesia was ever needed. Parameters of blood coagulation, International Normalized Ratio (INR, lower than 1.5) and activated Partial Thromboplastin Time (aPTT, lower than 1.5) were examined as a standard before the procedure.

The intervention was intended according to a diagnostic imaging examination. The safest needle approach to reach the lesion was defined. The needle track was planned to avoid bladder, small and large bowel, vessels, and expected nerves pathways. The entry point was defined by placing a skin mark. The length and angle of the biopsy needle were measured on the basis of an intraprocedural CT imaging with a local anesthesia needle. This step is essential for the actual assessment of the needle position and the localization of the lesion and surrounding structures. The procedures were carried out using the half-automatic biopsy system (Palium biopsy, M.D.L. SRL, Delebio, Italy). The expected needle entry was disinfected and standardly covered with sterile drapes. In accordance with the selected course, a 14 G / 16 G / 18 G of 10 cm / 16 cm / 20 cm length with a 22 mm throw needle was inserted into the lesion. After obtaining the specimen, the needle was carefully extracted from the appropriate pelvic part. The samples were put into a sterile 4% formaldehyde solution and the transport system for subsequent examinations. In all cases, a one-step approach was used.

After the intervention, one series of CT scans in the same ranges as in the preprocedural examination was performed to exclude the possibility of early complications. The needle puncture mark was disinfected and covered with sterile plaster. The duration of the complete intervention never exceeded 30 min. The patients were transported to the standard department of gynecology, urology or oncology because of the vital functions monitoring possibility. The upcoming day, they were discharged from the departments after laboratory, clinical, and ultrasound examinations.
After following surgical therapy, histopathological results were compared after the biopsy and after the resection approach. It was considered a success if the relations between the results were identical. In non-surgically treated patients (benign histological findings, disseminated malignancies or lymphomas), histological results were compared with known tumorous diseases in their medical history and the outcomes of the appropriate treatments. If, despite the therapy, disease progression was verified and the patient died, the autopsy histological results were compared with outcomes of the biopsies. For the follow-up, CT (identical CT device), PET/CT Discovery VCT 64 (General Electric Healthcare, Milwaukee, Wisconsin, USA) or magnetic resonance Siemens Magnetom Avanto 1.5 Tesla (Siemens, Forchheim, Germany) were used.

Final histopathological results were supplemented with subtyping in the majority of cases. The treating physicians, especially oncologists, made the decisions for the subtyping extent. In proved cases of colorectal carcinoma, mutation of the genes BRAF and RAS were required, in renal cell carcinoma, individual histological subtypes and also nucleolar or nuclear grading were defined, in prostate adenocarcinoma a Gleason score was determined. Immunohistochemical examinations were indicated in all verified breast carcinoma cases due to the occurrence of hormonal receptors.

In non-Hodgkin lymphomas, subtyping was completely fundamental. The detailed differentiation of aggressive subtypes – diffuse large B-cell lymphoma (DLBCL) or mantle cell lymphoma (MCL) – and indolent subtypes – chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), anaplastic large cell lymphoma (ALCL) or marginal zone lymphoma (MZL) – determined the therapy and assessed the prognosis. Follicular lymphoma was a special category especially due to the correct grading determination in grades 2, 3A and 3B. In Hodgkin disease, individual subtypes were determined.

If, despite a negative histological result, a malignant disease was still suspected, a surgical diagnostic approach was indicated for obtaining adequate tissue specimen. The next percutaneous bioptic attempt was never used. In 4 patients two procedures were performed on the same patients, but from different pelvic locations, at various time intervals and with distinct final histological results.

The retrospective data collection was used for the study. Median and interval data were used for the basic quantitative statistical evaluation. These data were correlated with other qualitative monitored parameters using Fisher’s exact tests. Qualitative statistical data were descriptively evaluated and compared with quantitative parameters. For the evaluation of unpaired data, a nonparametric Mann-Whitney test was used. The statistical importance was established at level $p = 0.05$. The statistical software NCSS 11 (NCSS, LLC, Kaysville, Utah, USA) was used.

Results

A total of 140 biopsies with accessible histopathological results were integrated in the study. 140 interventional procedures were performed in 136 patients. The patients were women in 77 cases (56.6%) and men in 59 cases (43.4%), aged 21 to 87 years (median age 65 years). The interventions were carried out in different pelvic levels for tumors ranging from 17–160 mm in the largest diameter (median size 53 mm). In total,
in 5 procedures were histological outcomes considered false negative (3.6%). In 135 biopsies (96.4%) results were considered true positive or true negative. In 79 cases (56.4%) malignant disease was preprocedurally known in a patient’s clinical history.

Histologically, the most common diagnosis was metastatic disease to the various pelvic parts or lymphatic nodes, occurring in 37 cases (26.4%). Metastatic disease was defined as a verified histological diagnosis equal to known malignancy in a patient’s clinical history. Metastatic impairment of upper gastrointestinal malignancies was diagnosed in 7 cases (5%), i.e. Krukenberg tumors. In 35 cases the final results were lymphomas (35 of 140 procedures; 25%). DLBCL was the most commonly revealed subtype. As the initial diagnosis the lymphoma was verified in 11 cases; as relapse or transformation in 24 procedures. Other diagnoses were verified less frequently. No tumorous cells were proved in a total of 23 procedures (16.4%). Tables 1 and 2 show a detailed overview.

| Diagnosis                  | Number |
|----------------------------|--------|
| Metastatic disease         | 37     |
| Serous adenocarcinoma      | 22     |
| DLBCL                      | 15     |
| Follicular lymphoma        | 4      |
| Plasmacytoma               | 4      |
| Neurinoma                  | 3      |
| ALCL                       | 3      |
| CLL/SLL                    | 2      |
| Hodgkin lymphoma           | 2      |
| Marginal zone lymphoma     | 2      |
| Ganglioneuroma             | 2      |
| Melanoma                   | 2      |
| Serous adenofibroma        | 2      |
| Leiomyoma                  | 2      |
| Dedifferentiated carcinoma | 2      |
| Mantle cell lymphoma       | 1      |
| T-cell non-Hodgkin lymphoma| 1      |
| Pleomorphic sarcoma        | 1      |
| Granulosa cell tumor       | 1      |
| Osteosarcoma               | 1      |
| GIST                       | 1      |
| Neuroendocrine tumor       | 1      |
| Leiomyosarcoma             | 1      |
| Lipoleiomyoma              | 1      |
| Thecofibroma               | 1      |
| Acute myeloid leukemia     | 1      |
| Epitheloid hemangiosarcoma | 1      |
| Adenosquamous carcinoma    | 1      |
| No tumorous cells verified | 23     |
| N                          | 140    |

ALCL, Anaplastic Large Cell Lymphoma; CLL/SLL, Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma; DLBCL, Diffuse Large B-Cell Lymphoma; GIST, GastroIntestinal Stromal Tumor.
As the preprocedural examination was CT used in 93 cases (66.4%), PET/CT in 25 interventions (25%), and magnetic resonance in 12 cases (8.6%). PET/CT was preferred in all patients with known lymphoma in medical history because of identification of the most viable tumorous part. This localization was then established as the most eligible for biopsy. Surgical approach was selected in 9 cases (6.4%). Skin to lesion distance varied from 27 cm to 165 cm (median length 51.5 cm). The Mann-Whitney test was used for evaluation of relationships among age, size, and skin to lesion by number of samplings, needle gauge and complications. This test proved statistically non-significant relationships among individual monitored parameters.

The 16 G needle was used in 113 procedures (80.7%), the 18 G needle in 21 biopsies (15%), and the 14 G needle in 6 cases (3.4%). The 16 G caliber was satisfactory for the majority of interventions. The lower needle caliber (18 G) was reserved for risky processes located near large vessels or gastrointestinal tract structures. The Fisher’s exact test revealed not a statistically significant relation between the hypervascular process and needle gauge ($p = 0.50208$). On the other hand, a statistically significant relationship between needle gauge and histological results accuracy was identified ($p = 0.00429$) due to the higher frequency of false-negative results when using the 18 G biopsy needle.

A supine position was used in 81 procedures (57.8%), a prone position in 49 biopsies (35%) and a side position in 10 (7.2%) interventions (Figure 1). The Fisher’s exact test confirmed a statistically non-significant relation between the patients’ position and complication rate ($p = 0.82739$).

The number of bioptic samplings was variable. One attempt in 15 interventions (10.7%), two attempts in 87 procedures (62.1%), three samplings in 29 biopsies (20.7%), and four samplings in 9 cases (6.5%) were performed. One attempt was determined especially for risky interventions near great vessels and the large or small bowel. Obtaining two samples was sufficient in the majority of procedures. More than three attempts were optimal for large masses with an emphasis on targeting different parts of the tumor. The Fisher’s exact test proved a statistically non-significant relation between the number of bioptic attempts, complication incidence ($p = 0.38109$) and accuracy of histological results ($p = 0.52902$).

### Table 2. The number of diagnosed metastatic diseases.

| Metastatic diagnosis              | Number |
|-----------------------------------|--------|
| Colorectal carcinoma              | 12     |
| Upper GI tract carcinoma          | 7      |
| Urothelial carcinoma              | 5      |
| Squamous cell carcinoma           | 4      |
| Renal cell carcinoma              | 3      |
| NSCLC                             | 2      |
| Endometrial carcinoma             | 1      |
| Cervical carcinoma                | 1      |
| Breast carcinoma                  | 1      |
| Prostate carcinoma                | 1      |
| N                                 | 37     |

NSCLC, Non Small Cell Lung Carcinoma.
The group of false-negative final results contained five patients. In three of these cases, the results were completely necrotic tissue, and in two cases biopsy verified low cellular mesenchymal tissue without any option of detailed classification. However, suspicion on malignant process occurrence still persisted and wide tumorous tissue excisions using surgical approach were performed. The final histological examinations revealed metastatic colorectal carcinoma 2 times, and in one case ovarian cystadenobroma, myxoid liposarcoma and leiomyoma with large areas of necrotic tissue. The procedure technique was standard, but the tissue specimen was biopsed from the non-viable parts of the processes (Figure 2).

In the group determined as the true negative, a detailed long-term follow-up was used. The shortest time interval was 24 months after the intervention. A total of 18 patients (18 of 140 procedures; 12.9%) were followed in this group. The most common benign histological result was a chronic inflammatory process in 10 cases. Lymphatic node with reparative changes was verified in 3 cases, radiation necrosis in 2 procedures and in one case each immunoglobulin G4-related disease (IgG4-RD), necrotising vasculitis and extramedulary hematopoiesis were revealed. All of these results were validated by
follow-up MR, CT or PET/CT examinations, where the processes remained without any treatment for more than two years either stationary, decreased in amount or totally disappeared (Figure 3). Surgical resection was indicated despite the negative result in four of these cases; the histological results were identical to percutaneous biopsies.

The complications were verified in 7 procedures (5%). All complications were bleedings (Figure 4) and were compared with the number of attempts, skin to lesion distance, needle gauge and vascularization. The statistical data analysis verified no significant relation between complication rate and the number of biotic attempts ($p = 0.38109$) and needle gauges ($p = 0.35509$). In the confirmed hemorrhages, 6 procedures were carried out on hypervascular masses. The Fisher’s exact test proved a statistically significant relation between the hypervascular process and complication rate ($p = 0.00004$). Conservative treatment was adequate in all cases. Blood transfusion was never needed. These patients stayed in the hospital for a total of two days.

**Discussion**

We report our results regarding CT-guided biopsy using a percutaneous approach and its applicability in the pelvic space. The overall accuracy was high not only in establishing

![Figure 2.](image-url) (A–D) The false negative result. Heterogenous process in the right parailiac region on contrast medium enhanced CT examination (A, curved arrow). Inserting of the biopsy needle (B and C, patient in prone position) into various tumorous parts using transgluteal approach. The final result was completely necrotic tissue. Surgical diagnostic procedure was indicated and metastatic colorectal carcinoma was revealed. Targeted systemic treatment was selected; follow-up CT examination 3 months after initial intervention verified tumorous process progression (D).
final histological diagnoses but also in subtyping. Metastatic disease and different lymphoma types were the most common verified diagnoses. The true negative results were considered the final diagnoses after surgical verification or long-term follow-up. A larger needle caliber of 16 G and at least two biopitic samplings were used in the majority of interventions. Statistically significant relationships between biopsy needle gauge and histological results accuracy, and between the skin to lesion distance, hypervascular process and complication rate were identified.

Historically, the surgical approach (simultaneously diagnostic and therapeutic) using general anesthesia, laparotomy or laparoscopy was performed with the emphasis on the most extensive tumorous tissue resection. Histological examination including subtyping and resection margins then proved the potential radicality and the origin of the process. This procedure carried all the risks of general anesthesia, resulted often in postoperative complications and prolonged recovery time, which was not sufficient for the early beginning of further systemic treatments.

Imaging-guided biopsy using a percutaneous or endoluminal approach provides another possibility for tumorous tissue sampling. These procedures are considered effective, safe, least demanding for the patients and without the need for general anesthesia. Since the initial experience of these procedures in the 1980’s, they have been widely

Figure 3. (A–D) The true negative result. Hypovascular mass left in pelvis on CT examination (A, arrow) in the venous phase and transversal plane. The insertion of the biopsy needle (B, patient in prone position). The histological result was necrotising vasculitis. The patient was treated with systemic corticosteroid therapy; follow-up CT examination after 6 (C) and 12 months (D) confirmed gradual partial and then complete regression of the process.
accepted in medical practice. A relevant exception to this approach is ovarian and adnexal masses, especially due to the risk of peritoneal seeding of tumorous cells. The initial diagnostics of adnexal tumors usually remains surgical. Percutaneous biopsy can be used in cases of imaging-proved disseminated malignancy with high suspicion of ovarian origin, with no possibility of radical resection.

Aspiration biopsy procedures (Fine Needle Aspiration Biopsy - FNAB) and cytology can be useful in cystic masses, for exact solid tumorous tissue diagnostics, and moreover, subtyping, are not eligible. Core needle biopsy (CNB), as a diagnostic intervention able to repeatedly and safely obtain suitable tissue samples, is the most preferred minimally invasive procedure. CT guidance was initially widely used, but over the following decades it was gradually replaced by endoscopic (in cases of rectal cancer), ultrasound or magnetic resonance (in cases of prostate and cervical cancer) approaches. The clear advantages of CT guidance are the whole pelvis diagnostic coverage, unequivocal imaging documentation and safe biotic instruments pathway excluded unaffected structures injury. Ionizing radiation is on the other hand the most serious disadvantage.

Metastatic disease is the most common diagnosis of pelvic lesions; our results correspond to this fact. Metastatic tumors to the ovary that contain well-defined histological
characteristics and originate in the gastrointestinal tract are known as Krukenberg tumors. We identified these in 7 of 37 verified metastatic cases (18.9%). In our group, the incidence of metastatic disease and lymphomas was almost equal. The pelvis is frequently affected in cases of lymphoma transformation or relapse, but initial lymphoma presence is not common. Therefore, if the follow-up PET/CT confirms the most viable tumorous mass in the pelvic space, the location is then the most suitable for the biopsy. The correct localization for biopsy plays a decisive role in verifying exact histological results and overall accuracy. Nevertheless, the surgical approach is still slightly superior to needle biopsy in diagnostics of lymphoma transformation.

In literature, there is an indeterminate relationship between bioptic needle gauge and improved diagnostic accuracy. In general, a thicker needle allows for more tumorous tissue amounts to be obtained and more histopathological examinations can be performed. The use of a 18 G needle is the most referred bioptic instrument in scientific articles. In our study, a 18 G needle was used only in 15% of cases; in 85% of procedures we found the 16 G or wider needle more suitable. The complication incidence was identical. Simultaneously, the biopted tissue quantity was larger, therefore we find wider bioptic instruments to be more eligible. The complication rate is reported at around 5%; our results correspond to this level. Our only complication was bleeding; biopsies performed through the rectal or vaginal wall can be complicated infectiously, also up to 5%.

Different articles can be found regarding pelvic processes diagnostics using various needle gauges, approaches and imaging guidance. The initial published articles yielded ca. 80% accuracy; subtyping rates were not determined. Large amounts of pelvic tumorous processes in the population led to the development of many improved diagnostic methods. Recently presented studies declared both overall and subtyping accuracies exceeding 90–95%. These results approximate those of surgical excisions and endoluminal approaches. Our results correspond and slightly exceed these published data. Simultaneously, endoluminal diagnostic approaches are preferred in medical practice, especially due to their clear advantages – the possibility of real-time procedure control possibility, absence of ionizing radiation and gradual availability for clinical physicians. On the other hand, endoluminal approaches cannot reach all pelvic anatomical parts and here we find the indications for CT guidance.

The limits of our study are the single-center data collection, retrospective data analysis, which depends on the hospital information system and the absence of a control group. The number of engaged patients is comparable to or higher than other published articles.

In conclusion, core needle biopsy using a percutaneous approach and CT guidance has high overall accuracy not only in establishing the correct final diagnosis of pelvic lesions, moreover also in its subtyping. This technique is reserved for cases in which the process is not clearly seen with sonography or when a safe pathway to the lesion is not found using other possible guidances. Core needle biopsy, using at least two samplings of 16 G or a wider caliber, is well-tolerated by the patients, has a low complication rate and can be performed routinely in the pelvic space as an equal procedure to other used approaches.
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Author contributions
PH, PD: biopsy performing, manuscript writing, final approval; MB, JS, AR: data analysis, following-up; MH, JV: literature search, data analysis.

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ORCID iD
Petr Hoffmann https://orcid.org/0000-0001-5133-2572

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Author biographies

Petr Hoffmann is a research fellow at the Charles University. He has been working at the University Hospital Hradec Kralove. He received his PhD in renal ablation interventions. His work focuses on the interventional procedures especially in the abdominal cavity and the pelvis.
His articles are recognized at national and international levels. Also, he is serving as reviewer of various well reputed international journals.

Michal Balik is a physician at the department of Urology at the University Hospital Hradec Kralove. He is engaged in a broad spectrum of pelvic surgical procedures including robotic resections.

Martina Hoffmannova is a lector at the faculty of Education in Hradec Kralove. She works in various research groups with focusing on data analysis using also excellent language skills.

Jiri Spacek is a physician at the department of Urology at the University Hospital Hradec Kralove. He is specialized in a comprehensive spectrum of urological issues including surgical procedures.

Jiri Vanasek is a physician at the department of Radiology at the University Hospital Hradec Kralove. He is a part of research groups with engaging in general diagnostic radiology, oncology and interdisciplinary councils.

Adam Rezac is a physician at the department of Gynecology and Obstetrics of the University Hospital Hradec Kralove. His specialty is a gynecologic oncology and surgical treatment of these diseases.

Petr Dvorak is an Associated Professor at the Charles University. He has been working at the department of Radiology of University Hospital Hradec Kralove. His work focuses on the non-vascular interventional procedures especially using CT guidance and is well known at national and international levels.