Sciatic nerve: beyond the sacral foramen

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ABSTRACT
Sciatica may result from pathologies affecting the nerve both in its intraspinal and extraspinal course. In daily routine, the vast majority of cases are caused by herniation of the lumbar discs compressing the neural roots. Extraspinal causes of sciatic pain are usually underestimated and the imaging study may be completed after reporting the lumbar MRIs. However, early diagnosis of the exact etiology of sciatica is paramount for both relieving the symptoms and preventing any additional neurologic injury. In this pictorial assay, some relatively rare causes of sciatic neuralgia along the route of the sciatic nerve after leaving the sacral foramen will be displayed.

In daily clinical practice, it is not rare to encounter patients with neurogenic claudication emanating from the abnormalities of the lumbosacral spine, mostly secondary to disc diseases, compression osteophytes, or spinal canal stenosis (1). Another subgroup with radicular pain of sciatic nerve (SN) have nothing to do with lumbosacral spinal etiologies but may be affected by pathologies beyond the sacral foramen, along the nerve path before, through, and after the sciatic foramen.

This study will review the anatomy of the SN after the sacral foramen through deep gluteal space on magnetic resonance imaging (MRI), with pathologies either belonging to the nerve itself or tissues in its vicinity causing sciatic neuralgia in this route.

Anatomical landmarks
The SN is formed by the L4–S3 nerve roots leaving the sacral foramen, it lies antero-inferiorly to the sacroiliac joint and the piriformis muscle through the greater sciatic foramen (2). After the ischial spine, in the lesser sciatic foramen, the nerve extends between obturatorius internus muscle anteriorly and gluteus muscle posteriorly. At the level of the ischial tuberosity medially, the nerve can be identified in the subgluteal space, where the anterior border is formed by quadratus femoris and the posterior border by gluteus maximus muscles (3). Down to the posterior aspect of the thigh, SN travels between the biceps femoris and the adductor magnus (Fig. 1). Right above the knee level, it branches off into the common peroneal and tibial nerves.

Clinical findings
Other than pain radiating from the lower back down to the leg and foot, patients may experience either deep gluteal syndrome findings or secondary findings of denervation in the territory of the SN. The most common symptoms of deep gluteal syndrome include: hip or buttock pain; tenderness in the gluteal and retro-trochanteric region; sciatica-like pain, often unilateral but sometimes bilateral, exacerbated with rotation of the hip in flexion and knee extension; intolerance of sitting more than approximately half an hour; and lumbago (3). Biceps femoris, semitendinosus, semimembranosus, ischiocondylar part of adductor magnus, and all muscles below the knee can display denervation findings, as these muscles are supplied by SN.

MRI technique
Magnetic resonance neurography protocols prescribed for the SN both on 1.5 T and 3.0 T systems have been reported before (1). Magnetic resonance neurography relies on high-resolution (2–3 mm section thickness) T1-weighted spin echo (SE)/T1-weighted flu-
id-attenuated inversion recovery images and T2-weighted fat-saturated SE/spectral-attenuated inversion recovery (SPAIR)/short-tau inversion recovery (STIR) images in multiple planes. While STIR works best at 1.5 T, SPAIR with varying flip angles is preferred in 3.0 T systems, owing to a higher signal-to-noise ratio compared with STIR images (4). High-resolution MRI techniques are of utmost help in demonstrating the fibrous bands around the SN, which may be the cause of diminished sciatic mobility during hip and knee movements with the precipitating cause of sciatic neuropathy (3). Three-dimensional sequences with the addition of STIR have been routinely used in clinical practice for many years.

As stated before, on fluid sensitive sequences, increased nerve signal intensity approaching to that of neighborhood vessels may indicate neuropathy. In addition, enlargement of the nerve and abnormal fascicules are further indicators for neuropathy. Denervation changes such as edema, fatty infiltration, and atrophy of the related muscles may accompany sciatic neuralgia and may even be considered the first imaging proofs of disease. However, absence of these secondary findings cannot totally exclude possible SN pathology.

Pathologies proximal to the sciatic foramen

Beyond the sacral foramen in its pelvic extension anterior to the sacroiliac joints,

Main points

• Sciatic nerve (SN) pathologies may present with pain radiating from lower back down to the leg and foot, deep gluteal syndrome clinics, or secondary findings of denervation in the territory of the nerve.

• SN pathologies can be recognized either by the changes of the nerve itself such as increased signal intensity on fluid sensitive sequences, enlargement, and abnormal fasciculations, or by denervation changes in the related muscles such as edema, fatty infiltration, and atrophy.

• Distal to the sacral foramen, anatomical landmarks in the course of the SN such as the greater sciatic foramen (antero-inferiorly the sacroiliac joint and the piriformis muscle), the lesser sciatic foramen (obturatorius internus muscle anteriorly and gluteus maximus (GM) posteriorly), and the subgluteal space (quadratus femoris anteriorly and gluteus maximus muscle posteriorly) may enhance the understanding of different pathologies of the nerve.

SN may be affected by any pelvic soft tissue and bone tumors (Fig. 2); hematoma (Fig. 3); abscess formation mainly in the setting of sacroiliitis, either secondary to nonspecific agents or specific infections such as brucellosis or tuberculosis (Fig. 4); or inflammation and osteoarthritic changes of the sacroiliac joints, either through compression, invasion, or encroachment of the nerve with these disease processes.

Piriformis syndrome

Piriformis syndrome is another cause of pain radiating from the sacrum through the

Figure 1. a–d. Coronal T1-weighted image (a) shows the right-sided sciatic nerve (SN) leaving the sacral foramen and continuing inferolaterally through the pelvis and the sciatic foramina (arrows). Oblique-sagittal T1-weighted image (b) at the level of the greater and lesser sciatic foramina with piriformis (P) muscle the landmark of the greater sciatic foramina. The lesser sciatic foramen contains the obturator internus muscle (OI) anteriorly and gluteus maximus (GM) posteriorly. Note the extension of the SN anteriorly to piriformis muscle down to lesser sciatic foramen (arrow). Axial T1-weighted image (c) at the level of the infragluteal region shows the ischial tuberosity and the greater trochanter of the femur. The SN (arrow) extends between the quadratus femoris (QF) muscle and gluteus maximus muscle in this image. Axial T1-weighted image (d) at the mid level of the femur. The SN (arrow) lies in between the adductor magnus and biceps femoris (BF) muscles.

Figure 2. A 22-year-old male with lymphoma involving the sacrum and the right pelvic ring. The SN, in its extension in the pelvis through the sciatic foramen, is hard to identify in the soft tissue component/edema of the tumor as a separate structure at its expected location (arrow).
gluteal area and down to the posterior aspect of the thigh, caused by an abnormal condition of the piriformis muscle. The possible causative factors for this syndrome are traumatic injury and reflex spasm of the muscle, which results in edema and contractures with subsequent compression and entrapment of the SN (5). Hypertrophy of the muscle, dynamic entrapment of the nerve by the muscle, and an anomalous course of the SN due to anatomical variations are the other etiologies for piriformis syndrome (3). As an adjunct to clinical diagnosis, MRI plays a role in revealing an enlarged or anomalous muscle with changes in the SN (5) (Fig. 5).

Pathologies through the sciatic foramen

Trauma neuropathy

Pilates is a technique that aims to improve the core strength and flexibility through six basic principles of balance, concentration, control, precision, breathing, and flow. It is reported that when practiced correctly, some Pilates exercises can relieve sciatic pain (6). Although it is unlikely that Pilates may cause sciatica, certain exercises might exacerbate a preexisting sciatic condition (7). The female case displayed in Fig. 6 presented with pain on her left buttock, and had a history of Pilates exercises she had been performing on her own. The SN shows hyperintensity in a short segment, which is found compatible with neuropraxia according to the given history. Neuropraxia is the lowest degree of damage of the myelin sheath surrounding the axon causing transient functional loss, with an excellent prognosis. On MRI, neuropraxia is seen as mild thickening of the nerve with hyperintensity on fluid sensitive sequences.

Postinjection sciatic neuropathy

Postinjection sciatic neuropathy is a disorder caused by an improper technique of injection or the introduction of a medicinal agent into the gluteal region. Either a direct puncture of the SN or an adjacent blood vessel by an injection needle or compression of the nerve by a hematoma can be the cause of the injury. The spectrum of neurologic presentation ranges from minor transient pain to severe sensory disturbance and even motor loss. Early recognition of the nerve injection injury and appropriate management via drug treatment aiming pain relief, physiotherapy, and surgical exploration are needed to prevent neurologic deficits. On T2-weighted images hyperintense intraneural lesion, entirely or partially involving nerve fascicles, is reported as the main imaging criterion (Fig. 7) (8).
Pathologies distal to the sciatic foramen

Paradoxic hypertrophy

Paradoxic SN hypertrophy may occur after a lower limb amputation performed for both malignant and nonmalignant conditions. Hypertrophy is reported to be greatest near the transection site extending proximally. It is termed paradoxical because usually transection of the limb is followed by atrophy of the nerve instead of hypertrophy. The etiology remains unclear; however, some propose that it may be secondary to dysregulated axonal neurofilament transport (9). Differentiating this benign process from a residual or locally recurrent tumor may prevent unnecessary biopsies (Fig. 8) (9).

Posttraumatic neuroma

Neuroma is a non-neoplastic proliferation at the end of an injured nerve, usually 1–12 months following the amputation. Two types of postamputation neuromas are encountered: terminal neuroma (end-bulb), which originates at the end of the injured nerve, represents a normal healing pattern of the nerve and is often asymptomatic; while, spindle neuroma (neuroma-in continuity) is localized within the nerve, away from the injured nerve ending. While the first pathology occurs in a completely transected nerve, which is not in apposition with the distal nerve, the latter displays a fusiform thickening of the nerve due to injury or chronic friction of the intact nerve (Fig. 9) (10). Patients cannot always point the pain when there is neuroma, making it difficult to distinguish from phantom limb pain. Soft tissue mass and pain generated by percussion on stump are among the possible clinical findings. Pain relief after injection of lidocaine to the painful area may help confirm the diagnosis.

Localized hypertrophy

Localized hypertrophic neuropathy of the SN in children is a rare condition, presenting with entrapment neuropathy in the territory muscles of the SN (11). The findings can be summarized as i) segmental, focal enlargement of the SN; ii) increased hyperintensity of the effaced nerve segment on T2-weighted images; iii) ”salt and pepper” appearance of the segment indicating the preservation of fascicular configuration; and iv) possible enhancement after intravenous gadolinium administration (Fig. 10) (11). Pathology of the swollen nerve segment reveals onion-bulb like formations of perineural cells giving the nomenclature of localized hypertrophic neuropathy. This condition should be among the differential diagnoses for several etiologies of monomelic amyotrophy.

Entrapment secondary to vascular prominence

Vascular lesions such as venous angioma, arteriovenous malformation, venous malformations in the setting of Klippel-Trenaunay syndrome, and capillary hemangioma in the vicinity of the SN may be the cause of sciatica (12). In the case presented in Fig. 11, the dilated vascular segment may cause pressure over SN, particularly in certain body positions.

Bony trauma

Although the frequently associated posterior luxation of the femoral head plays a more significant role in the SN injuries, acetabular fractures may also cause damage to the nerve. SN injury in the setting of acetabular fractures may result from i) initial direct damage; ii) during reconstructive surgery with intraoperative positioning and the usage of several instruments; or iii) as a late complication of surgery including wear debris, implant migration, hematoma, scarring, and heterotopic ossification. Patients with hip injuries and acetabular fractures should be evaluated for possible SN injuries. On MRI, muscular enlargement, edema, or scarring around the SN can be seen as a representation of the nerve injury (Fig. 12) (13).

Benign peripheral nerve sheath tumor

Schwannoma of the SN may originate at any level of the nerve from pelvis to thigh. These rare tumors of SN arise from the sheath of the nerve. Since schwannomas do not penetrate the nerve fascicles, their enucleation is possible, preserving nerve continuity. On the other hand, neurofibromas deeply affect the nerve and thus
require complete resection. Differential diagnosis between schwannoma and neurofibroma on MRI may help the surgeon to foresee the extension of his operation and its consequences. Classically, the nerve lies eccentric to the mass in schwannoma, but central or obliterated by the mass in neurofibroma (14). The “target sign”, low signal intensity centrally and high signal intensity peripherally at T2-weighted images, is more frequent in neurofibromas, although it may be seen in schwannomas as well. While

Figure 10. a, b. An 11-year-old boy with a complaint of weakness of the ankle dorsiflexion and eversion, which yielded a peroneal nerve compromise. Axial T1-weighted image (a) of the knee shows fatty atrophy indicating chronic denervation of the lateral compartment muscles (arrow). As the common peroneal nerve was extending uneventfully, MRI of the SN was recommended. On sagittal fat-saturated T2-weighted image (b), the SN is thickened with preservation of the fascicles seen as tiny hypointense dots on axial fat saturated T2-weighted images (not shown). Findings are compatible with localized hypertrophy of the SN in this case.

Figure 11. A 64-year-old female with left-sided buttock pain. Axial fat-saturated T2-weighted image shows an enlarged vessel (arrow) at the posterior aspect of the SN, which may be exerting pressure over the nerve.

Figure 12. Coronal T1-weighted image shows trauma to the SN and possibly fibrosis around the nerve (arrow) in the chronic stage caused by acetabular fracture in a male. Compare the findings with the left-sided normal SN.

Figure 13. A 47-year-old male with schwannoma. Sagital fat saturated T2-weighted image shows a well-defined hyperintense mass in the posterior supracondylar region of the knee, with the SN entering the mass (curved arrow).

Figure 14. Giant malignant nerve sheath tumor of the SN on the left amputated lower extremity of a 28-year-old female patient with neurofibromatosis type 1. Multiple neurofibromas are evident with their grape-like, target appearances on fat-saturated T2-weighted image.
schwannoma has a true capsule composed of epineurium, neurofibromas are rarely encapsulated (Fig. 13) (14).

**Malignant peripheral nerve sheath tumor**

Malignant peripheral nerve sheath tumor (MPNST) is uncommon and can be associated with neurofibromatosis type I. A comparison of 41 MPNST and 20 neurofibroma cases revealed four significant features useful for distinguishing between MPNST and neurofibromas: i) increased largest dimension of the mass; ii) peripheral enhancement; iii) perilesional edema-like zone; and iv) intratumoral cystic lesion (Fig. 14) (15).

**Conclusion**

Patients with SN pathologies may refer to MRI either with secondary findings of denervation in the related muscles or radicular pain in the territory of the nerve. If the MRI of the lumbosacral spine is not satisfactory to explain the present clinical setting, a dedicated SN MRI examination may be needed. On these images, SN should be tracked at those certain anatomical landmarks, and any change in signal intensity, thickness, fascicular arrangement should be evaluated. The presence of any adjacent bone and soft tissue pathologies should be investigated for possible adverse effect on the SN.

**Conflict of interest disclosure**

The authors declared no conflicts of interest.

**References**

2. Ergun T, Lakadamyali H. CT and MRI in the evaluation of extraspinal sciatica. Br J Radiol 2010; 83:791–803. [CrossRef]
13. Issack PS, Helfet DL. Sciatic nerve injury associated with acetabular fractures. HSS J 2009; 5:12–18. [CrossRef]
Radiologic findings of screen-detected cancers in an organized population-based screening mammography program held in Turkey

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PURPOSE
Breast Cancer Screening Program is a population based organized screening program in Turkey, where asymptomatic women aged 40–69 years are screened biannually. In this prospective study, we aimed to determine the mammographic findings of screen-detected cancers and discuss the efficacy of breast cancer screening in a developing country.

METHODS
A total of 6912 women were screened in three rounds. The radiologic findings were grouped as mass, focal asymmetry, calcification, and architectural distortion. Masses were classified according to shape, border, and density. Calcifications were grouped according to morphology and distribution. Cancers were grouped according to the clinical stage.

RESULTS
Seventy cancers were detected with an incidence of 4.8/1000. Two cancers were detected in other centers and three were not visualized mammographically. Mammographic presentations of the remaining 65 cancers were mass (47.7%, n=31), calcification (30.8%, n=20), focal asymmetry (16.9%, n=11), architectural distortion (3.1%, n=2), and skin thickening (1.5%, n=1). The numbers of stage 0, 1, 2, 3, and 4 cancers were 13 (20.0%), 34 (52.3%), 14 (21.5%), 3 (4.6%), and 1 (1.5%), respectively. The numbers of interval and missed cancers were 5 (7.4%) and 7 (10.3%), respectively.

CONCLUSION
A high incidence of early breast cancer has been detected. The incidence of missed and interval cancers did not show major differences from western screening trials. We believe that this study will pioneer implementation of efficient population-based mammographic screenings in developing countries.

Breast cancer is the most common cancer affecting women worldwide, with about 1.4 million new cases diagnosed each year (1). The incidence of breast cancer is about four-fold higher in developed countries (2). However, it has been shown that in low and middle-income populations, the number of breast cancer cases is increasing at a faster rate compared with high-income countries (3). In Turkey, breast cancer incidence is 46.8/100,000 and has more than doubled in the last two decades due to a westernizing lifestyle and aging (1, 4). The Breast Cancer Screening Program is a population-based organized screening program that began in 2008, in which asymptomatic women aged between 40–69 years are screened for 10 years biannually. In this prospective study, we aimed to determine whether the mammographic findings of screen-detected cancers correlated with histopathologic findings and discuss the efficacy of breast cancer screening in a developing country.

Methods
Study population
Screening mammography was performed in women aged 40–69 years who lived in .......... and who accepted the screening invitation. Pregnant women, women with a previous diagnosis of breast cancer and women who had a mammography in the last two years were excluded. Screening was registered to the Breast Cancer Screening Center between January 2009 and October 2014 every two years in three screening rounds. An approval by Institutional Review Board of .......... University was obtained. National Health Authorities...
were informed and approval was obtained. Each eligible woman signed a written informed consent form.

Screening procedure
A full-field digital mammography system was used (Selenia, Hologic). Bilateral mammograms were obtained including mediolateral oblique (MLO) and cranio-caudal (CC) projections. All examinations were double read by two independent radiologists (A. K. and O. C.) with eight years of experience who were blinded to each other’s interpretations. Mammographic findings and breast parenchymal patterns were assessed in accordance with the Breast Imaging Reporting and Data System (BIRADS) of the American College of Radiology (ACR) (Reston, 2003). The final decision was made according to the highest BIRADS score. When there was a discrepancy between the readers as to whether to follow-up or perform a histopathologic confirmation, the final assessment was determined in consensus. Women with mammograms categorized as BIRADS 0 (incomplete, need additional imaging assessment) were recalled for additional work-up including spot compression and magnification mammography, or ultrasonography (US). A follow-up US was performed to all women with type 3 and 4 breasts during a period not exceeding two weeks following the first round screening mammogram. The histopathologic confirmation for BIRADS scores of 4 and 5 lesions was made using a US-guided core (14-gauge) needle biopsy (n=20), vacuum assisted large core (11-gauge) stereotactic (VALCS) biopsy (n=1), wire-guided excisional breast biopsy (n=2), and excisional breast biopsy (n=37).

Outcome measurements
The women were grouped according to age as 40–49 and 50–69 years. For each breast, the localization of mammographically-detected abnormalities were grouped as upper-inner, upper-inner, lower-inner, and lower-inner quadrants, central, retroareolar, and axillary. The radiologic presentation of cancers were classified as mass, focal asymmetry, calcification, and architectural distortion.

Masses were classified according to their shape, border, and density. The shape of masses were grouped as round, oval, lobular, and irregular. The borders of masses were grouped as well-circumscribed, microlobular, obscured, irregular, and spiculated. The density of masses were classified as high, intermediate, low density, and fat-containing. Calcifications were grouped as heterogeneous, amorphous, pleomorphic, and fine linear according to their morphology. The distribution of calcifications were grouped as diffuse, regional, clustered, segmental, and linear. The presence or absence of axillary lymph nodes were noted. Mass was considered as the dominant finding in mammograms with a finding of mass associated with calcification. Cancers were also grouped according to the clinical stage to assess the distribution of early and invasive cancers as follows: stage 0 (in situ cancer), stage 1 and stage 2 (early invasive cancer), stage 3 (locally advanced cancer) and stage 4 (metastatic cancer).

The radiologic findings of interval cancers (cancer detected in women who were referred to the screening center with symptoms within one year of the last round with a negative mammogram) and missed cancers (cancer detected after a negative mammogram) were assessed.

Statistical analysis
The continuous distributions of variables were evaluated with Kolmogorov-Smirnov test. In addition, Spearman’s correlation analysis, chi-square test, Mann-Whitney U, and the Fisher-Freeman-Halton tests were performed. The statistical significance level was determined as P < 0.05. All analyses were performed using SPSS program version 11.0 (SPSS Inc.).

Results
A total of 6912 women were screened between January 2009 and October 2014, and 14485 bilateral mammographies were performed. A total of 70 cancers were detected, yielding an incidence of 4.8/1000. Two cancers were detected in other centers but the radiologic findings could not be obtained. Three cancers were solely detected under US and could not be visualized on mammography. Therefore, the statistical analysis was performed on a total of 65 cancers.

The number of cancers detected in the 40–49-year age group and the 50–69-year age group were 32 (45.7%) and 38 (54.3%), respectively. Of 68 cancers, 39 (57.3%) were located in the right breast and 29 (42.6%) were in the left breast. Cancers were located in the upper OUTER quadrant (n=45, 66.2%), upper-inner quadrant (n=6, 8.8%), lower-inner quadrant (n=4, 5.9%), lower-outer quadrant (n=3, 4.4%), retroareolar (n=3, 4.4%), central (n=3, 4.4%), and axillary (n=4, 5.9%). Axillary lymphadenopathy was present in seven cases (10.2%) on mammogram.

In the first screening round, US was performed in women with type 3 and 4 breast parenchyma by the same radiologist who read the mammograms. All three cancers detected solely under US had type 3 breast parenchymal pattern, presenting a mass obscured by dense glandular parenchyma.

Of the 65 mammographically-detected cancers, the majority presented as a mass (n=31, 47.7%), followed by calcification (n=20, 30.8%), focal asymmetry (n=11, 16.9%), architectural distortion (n=2, 3.1%), and skin thickening (n=1, 1.5%) as shown in Table 1. Of the 32 cancers detected in women aged 40–49 years, three were not visible on mammogram and were detected solely under US. The mammographic presentation of the remaining 29 cancers were as follows: mass (n=3, 44.8%), calcification (n=10, 34.5%), focal asymmetry (n=5, 17.3%) and architectural distortion (n=1, 3.4%). In women aged 50–69 years, 38 cancers were detected of which, two were detected in external centers and radiologic findings could not be obtained. The mammographic findings of the remaining 36 cancers were as follows: mass (n=18, 50.0%), calcification (n=10, 27.8%), focal asymmetry (n=6, 16.6%), and architectural distortion (n=1, 2.8%). In one woman (2.8%), only skin thickening was detected (Table 1).

Two patients presented with focal asymmetry associated with calcifications; these
patients were included in the calcification group because the calcifications were more remarkable. The characteristics of cancers presenting with a mass and calcifications are shown in Table 2. In one patient with a type 4 breast parenchyma, the only mammographic finding was skin thickening. Cancer was detected using US, which revealed a periareolar irregular solid mass.

The distribution of histopathologic types of cancers are shown in Table 3. Cancers were staged as stage 0 (n=13, 20.0%), stage 1 (n=34, 52.3%), stage 2 (n=14, 21.5%), stage 3 (n=3, 4.6%), and stage 4 (n=1, 1.5%). Of the total stage 0 and 1 cancers, 15 (31.9%) presented as calcifications, whereas 22 (46.8%) presented as a mass.

The radiologic and histopathologic correlation of tumor dimension was evaluated only for masses. The median diameter of 31 mammographically-detected masses was 16 mm (range, 6.0–47 mm), whereas the histopathologic median tumor diameter was 15 mm (range, 5.0–35 mm). Therefore, the radiologic assessments significantly correlated with the pathologic findings (r=0.675, P = 0.0001). The distribution of 6912 mammograms according to parenchymal pattern type 1, 2, 3, and 4 was 41.1%, 40.9%, 15.8%, and 2.2%, respectively. The breast parenchymal patterns of the 56 breast cancer patients that were detected in our center were as follows: type 1 (n=15, 26.8%), type 2 (n=36, 64.3%), type 3 (n=3, 5.4%), and type 4 (n=2, 3.6%). Cancers that presented as a mass were mostly seen in type 2 breast parenchymal pattern followed by types 1, 3, and 4, respectively. Calcifications were mostly seen in type 2 followed by type 1, type 4 and type 3, respectively. The distribution of radiologic findings according to breast parenchymal pattern is shown in Table 4. Of the 68 cancers, 56 (82.4%) were detected in routine screening rounds, five (7.4%) were interval cancers and seven (10.3%) were missed cancers.

Of five patients with interval cancers, one patient (20%) with symptoms of breast pain was seen at our screening center four months before her routine screening round, and a focal asymmetry in a type 1 breast parenchymal pattern was detected on a follow-up mammogram. Two interval cancers (%40) were detected in type 2 breast parenchyma. Of those, one was detected in an external center one month before the third screening round, which presented as calcification. The second woman had a palpable breast mass one year following the screening before the round was completed, and a de novo mass was detected in the follow-up mammogram (Fig 1). One (20%) interval cancer, which was detected in a type 3 breast, presented as a palpable mass six months before the second round. Finally, one of the interval cancers was detected

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**Table 1.** Distribution of radiologic findings of screen detected cancers according to the age groups

<table>
<thead>
<tr>
<th>Radiologic presentation of cancers (n=65)*</th>
<th>40–49 years</th>
<th>50–69 years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>40–49 years</td>
<td>13 (44.8)</td>
<td>18 (50.0)</td>
<td>31 (47.7)</td>
</tr>
<tr>
<td>50–69 years</td>
<td>10 (34.5)</td>
<td>10 (27.8)</td>
<td>20 (30.8)</td>
</tr>
<tr>
<td>Total</td>
<td>23 (100.0)</td>
<td>28 (100.0)</td>
<td>51 (100.0)</td>
</tr>
</tbody>
</table>

No significant difference was found between the age groups (P = 0.984, Fisher-Freeman-Halton test).

*Three cancers could not be visualized on mammography, while two cancers were detected in other centers and the radiologic findings could not be obtained.

**Table 2.** Characteristics of screen-detected cancers that presented as mass and calcification

<table>
<thead>
<tr>
<th>Mass (n=31)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shape</td>
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</tr>
<tr>
<td>Irregular</td>
<td>26 (83.9)</td>
</tr>
<tr>
<td>Round</td>
<td>3 (9.7)</td>
</tr>
<tr>
<td>Oval</td>
<td>2 (6.4)</td>
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<tr>
<td>Margin</td>
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</tr>
<tr>
<td>Spiculated</td>
<td>15 (48.4)</td>
</tr>
<tr>
<td>Irregular</td>
<td>14 (45.2)</td>
</tr>
<tr>
<td>Well-defined</td>
<td>2 (6.4)</td>
</tr>
<tr>
<td>Microlobular</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Obscured</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Density</td>
<td></td>
</tr>
<tr>
<td>Dense</td>
<td>19 (61.3)</td>
</tr>
<tr>
<td>Intermediate density</td>
<td>10 (32.3)</td>
</tr>
<tr>
<td>Low density</td>
<td>2 (6.4)</td>
</tr>
<tr>
<td>Fat containing</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Calcification (n=20)</td>
<td></td>
</tr>
<tr>
<td>Type</td>
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<tr>
<td>Pleomorphic</td>
<td>8 (40.0)</td>
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<td>Heterogeneous</td>
<td>6 (30.0)</td>
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<tr>
<td>Amorphous</td>
<td>6 (30.0)</td>
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<tr>
<td>Fine linear</td>
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<td>Distribution</td>
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<tr>
<td>Segmental</td>
<td>15 (75.0)</td>
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<td>Regional</td>
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<td>Linear</td>
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</table>
in a patient with a complaint of nipple discharge in a type 4 breast nine months after screening, and presented with retroareolar focal asymmetry.

Of the seven missed cancers, one (14.3%) was detected in a type 1 breast parenchymal pattern that presented as focal asymmetry. It was misinterpreted as asymmetric glandular parenchyma following a spot compression mammogram. Three missed cancers (42.9%) were detected in type 2 breast parenchyma. Of these three, two presented as a mass and one presented as an architectural distortion. The remaining two (28.6%) were detected in type 3 and one (14.3%) in type 4 breasts, and all presented as calcification (Fig 2).

**Discussion**

Accurate preoperative detection of tumor size plays a major role because the surgical approach depends on the relation between tumor size and breast size, particularly when planning breast conservation therapy or neoadjuvant chemotherapy (5). According to the guidelines, histologic examination is the gold standard for the accurate tumor dimension measurements. However, mammography and US examinations are taken into consideration in deciding the therapeutic approach and can be supported by magnetic resonance imaging in selected cases (6, 7). In our study, there was a significant correlation between mammographic and histologic tumor size in women aged 50–69 years. However, accurate measurement of the lesions was reported to be difficult in mammograms due to tissue superposition and the lesion masking effect of two-dimensional imaging (7). We believe that the decreased parenchymal density in this age group had an incremental role in accurate measurement of tumor size.

The correlation between the mammographic appearance of the tumors and prognosis has become especially important after settlement of organized screening programs that enable earlier detection of

**Table 3. Histopathologic types of screen-detected cancers**

<table>
<thead>
<tr>
<th>Histopathologic type of cancers</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive ductal</td>
<td>41 (58.6)</td>
</tr>
<tr>
<td>DCIS</td>
<td>12 (17.1)</td>
</tr>
<tr>
<td>DCIS intracycstic papillary carcinoma</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Invasive lobular</td>
<td>10 (14.3)</td>
</tr>
<tr>
<td>Mixed</td>
<td>2 (2.9)</td>
</tr>
<tr>
<td>Tubular carcinoma</td>
<td>3 (4.3)</td>
</tr>
<tr>
<td>Mucinous carcinoma</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Total</td>
<td>70 (100)</td>
</tr>
</tbody>
</table>

**Table 4. Distribution of radiologic findings of screen detected cancers according to breast parenchymal pattern**

<table>
<thead>
<tr>
<th>Radiologic findings (n=65)</th>
<th>Breast density n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type 1</td>
</tr>
<tr>
<td>Mass</td>
<td>9 (56.3)</td>
</tr>
<tr>
<td>Calcification</td>
<td>4 (25.0)</td>
</tr>
<tr>
<td>Focal asymmetry</td>
<td>3 (18.8)</td>
</tr>
<tr>
<td>Architectural distortion</td>
<td>0</td>
</tr>
<tr>
<td>Skin thickening</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>16 (100)</td>
</tr>
</tbody>
</table>

**Figure 1. a–d. Left negative mammogram with a type 2 parenchymal pattern in an asymptomatic woman in 2011 (a, b). In 2012, a developing mass was detected in the upper-outer quadrant with an obscured inferior medial border (c, d).**
The characteristic mammographic presentations of breast cancer include mass, microcalcification, architectural distortion and focal asymmetry. Tumors with different clinical and pathologic characteristics have different mammographic manifestations that lead to variable prognoses. It has been stated that mammographic features can accurately be used as independent predictors for long-term outcome with a recommendation that the mammographic features of breast cancer should be taken into consideration during treatment planning especially for T1a and T1b tumors (8). Although the screening programs are successful in detecting small tumors leading to good prognosis, there is still a small number of women who die of early tumors. Tabar et al. (8) showed that women with casting microcalcifications had a poor prognosis and proposed that these women should undergo adjuvant chemotherapy. In our study, cancers that presented as calcifications were mostly pleomorphic with a segmental distribution. Additionally, the majority of tumors that presented as calcifications were Stage 0 and 1 tumors. However, tumors that presented with mass or focal asymmetry were mostly stage 1 cancers marking a little right shift. According to our data, in screen-detected cancers, the earliest tumors were those that are presented with calcifications. Screen-detected tumors presenting with calcifications may have a more favorable prognosis because calcification is thought to be one of the possible indicators of the presence of early breast carcinoma (9). We believe that this finding may be evaluated in more comprehensive screening series.

In our study, the screened women were grouped according to age distribution as 40–49 years and 50–69 years, and the distribution of mammographic features were delineated accordingly. The number of tumors that presented as a mass was slightly higher in women aged 50–69 years. The second most remarkable radiologic finding was calcification, which showed a higher proportion in women aged 50–69 years. The second most remarkable radiologic finding was calcification, which showed a higher proportion in women aged 50–69 years.

In our study, not all types and distributions of calcifications were detected. There were no cases with clustered and fine-linear calcifications as well as diffuse distribution. We believe that this was due to the limited number of screen-detected cancers, which may be considered as a limitation of our study.

In our study, 7.4% of the cancers were detected in the interval period between two

Figure 2. a–c. Left craniocaudal and mediolateral oblique mammograms with a type 3 parenchymal pattern. The segmented pleomorphic microcalcifications in the upper-outer quadrant were missed by two readers (a, b). Panel (c) shows the retrospective digitally magnified view of the missed calcifications.
search Frequency Trial, granular microcalcifications and deformity were two of the three most frequent presentations of missed cancers in screened women (21). In another study with a large number of screen-detected tumors in women aged 40–48 years, calcification and deformity were the most frequently detected signs (22). We retrospectively detected that calcifications were missed due to misinterpretation and the tendency of the readers to follow-up rather than take action for histopathologic confirmation. In accordance with the literature, the next most frequent presentation of missed cancers was a mass in our study. For mass lesions, an additional US was performed, and we think that, due to a similar reason as with calcifications the readers probably interpreted the masses as benign and a short-term follow-up was performed. We believe that our findings might be confirmed in the following rounds with higher numbers of screen-detected cancers.

Since sensitivity of mammography decreases in dense breasts, all women with type 3 and 4 parenchymal breast patterns underwent a follow-up US examination. A supplemental breast US in screened women increases the cancer detection rate by 2.391/1000 in women with dense breasts when compared with mammography alone (23, 24). We believe that US screening of dense breasts may have an incremental value for the detection of small and node-negative early cancers; a comprehensive series addressing the value of adding US in the survival of these women is required.

Delayed diagnosis of breast cancer is a crucial factor that increases mortality rates. Population-based organized screening studies have shown that the burden of breast cancer has decreased after the implementation of these screens in developing countries (25). With the introduction of mammographic screening, breast cancer is detected in earlier stages, with a tendency towards more favorable prognosis. This, in turn, will lead to a more gentle therapeutic approach, hence decreasing the use of chemotherapy. In the current study, most of the breast cancers were detected at earlier stages. We believe that this finding could be used as a basis to construct organized screening programs in developing countries.

The limitations of this study are.....

In conclusion, this is the first organized breast screening study in Turkey. Our breast cancer incidence was similar to those obtained in western screening trials; there were no major differences in terms of missed and interval cancer rates. Screen-detected breast cancers had different characteristics in younger and older age groups. We believe that this study will pioneer implementation of efficient population-based mammographic screening in other developing countries.

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Conflict of interest disclosure

The authors declared no conflicts of interest.

References

Results of a population-based screening mammography program held in Turkey