EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 6
Issue: 1
213-223
Year: 2019

BREAST IMAGING AND ITS CURRENT PROSPECTIVE

Rani Gupta Sah*[1-4], Arooj Aftab[1], Rajesh Prasad Sah[5], Pankaj Shah[6] and Jay Prakash[7]

[1]Calgary Stroke Program, Department of Clinical Neurosciences, University of Calgary.
[2]Seaman Family Centre, Foothills Medical Centre.
[3]Hotchkiss Brain Institute, University of Calgary.
[4]Department of Clinical Neurosciences.
[5]Department of Surgery, B.P Koirala Institute of Health Sciences, Nepal.
[6]Gandaki Medical College, Nepal.
[7]Himalayan White House International College.

***Corresponding Author: Rani Gupta Sah**
Calgary Stroke Program, Department of Clinical Neurosciences, University of Calgary.

Article Received on 25/10/2018 **Article Revised on 15/11/2018** **Article Accepted on 05/12/2018**

ABSTRACTS

Background: The imaging is crucial component not only for breast cancer screening, but also for diagnosis, evaluation, treatment, and follow-up of patients with breast cancer. **Methods:** The author reviews the current prospective and provides her personal views in describing the status of various imaging modalities such as mammography, computer-aided detection, ultrasonography dedicated magnetic resonance imaging, Magnetic resonance spectroscopy (MRS), positron-emission mammography and technologies under research for evaluating the breast detection and diagnosis. **Results:** Mammography is the unsurpassed screening modality for asymptomatic women and the initial imaging modality for symptomatic women. The advent of digital mammography may likely upgrade its sensitivity and specificity in women under 50 years of age and in those with dense breasts compared standard mammography. Computer-aided detection assists in experienced mammographers and enhances detection of microcalcifications in dense breasts. USG is used for characterization of the mammographic abnormality and for primary imaging of young women <30 years. Magnetic resonance elastography need further studies to establish their roles. Breast magnetic resonance imaging (MRI) provides anatomical and physiologic tissue features. It is useful in preoperative evaluation, clarification of indeterminate mammograms, and follow-up of BRCA mutation carriers. Contrast enhanced MRI is so far the most sensitive technology for the diagnosis of malignancy at the expense of reduced specificity. However. diffusion, and MR elastography have been applied to breast lesion characterization and show promise. The addition of MR Spectroscopy (MRS) can improve its specificity. In-vivo MRS is a valuable method to obtain the biochemical status of normal and diseased tissues. Malignant tissues contain a high concentration of choline-containing compounds that can be used as a biochemical marker. Molecular imaging can be useful in a select group of patients like those with suspected distant metastases, to evaluate loco regional extent, to detect the recurrence and monitor response to therapy. Positron-emission mammography promises enhanced detection of ductal carcinoma in situ, even when not associated with microcalcifications, and should aid surgical planning. Optical imaging and T Scan currently under research have potential to emerge as an adjunct to the existing technologies. **Conclusions:** This review presents the progress made in different imaging techniques in breast cancer screening, diagnosis and detection. The ideal modality for breast imaging should lead to early detection of cancer, free from adverse effects and cost effective. The advances in breast imaging have improved the sensitivity of detecting breast abnormalities. However, cost may be major limiting factors for the extensive application of some of these advances in the clinical backgrounds. The clinician needs to be aware of the benefits and weaknesses of each technology in order to apply them appropriately in evaluating their patients with breast problems in the clinical settings.

KEYWORDS: Breast cancer, Digital mamography, Computer aided diagnosis, Ultrasound, MRI, MR elastography (MRE), magnetic resonance spectroscopy (MRS), Molecular Imaging and Technologies under research.

INTRODUCTION

Breast cancer is one of the major causes of mortality in women globally (Torre et al. 2015). According to projections, about 24 million new breast cancer cases will be diagnosed by 2035, the incidence rates are high in developed countries, whereas the rates are low in less

developed countries. The disease affects thousands of Canadian women every year. Representing 26 percent of all cancers in women, breast cancer claims the lives of an estimated 5,300 Canadian women each year, and the Canadian Cancer Society estimates that one in nine women will develop breast cancer in her lifetime. Considering these staggering figures, women need more effective ways to detect this killer early. Imaging provides an optimal role to offer both screening and diagnostic tests for women at every degree of risk for the disease. With the advancement in technology it is postulated that decreasing breast cancer mortality may be due to increased use of mammographic screening, early detection of disease, availability of recent advancement in breast modalities. This article briefly describes the conventional and recent advances in breast imaging i.e Mammography, Ultrasonography, breast MRI, Molecular studies and Technologies under research.

Breast Imaging

Mammography: Remains the primary imaging method for breast screening and detection of breast cancer with sensitivity of around 75% but with variable specificity (Pisano et al. 2005). However, the sensitivity drops down to 50% in case of radiographic dense breast tissue, which is more common seen in younger women. (Pisano et al. 2005). It is proven to reduce breast cancer mortality by about 20% on long-term follow-up in randomized trials (Tabár et al. 2011, Oeffinger et al. 2015). It is also reported that this technique misses lesion around 10% to 25% of all breast cancers (Kim et al. 2011). The success of any screening program of asymptomatic women depends on the detection of subtle and small lesion. Limitation of mammogram includes exposure to ionizing radiation.

Digital Mammography Also called full-field digital mammography (FFDM) presently FFDM had entered the field with great promise. The newer technology of FFDM, despite its cost, clearly offers major advances in mammographic practice. FFDM allows for the decoupling and optimization of the processes of image acquisition, display, and storage. Digital imaging is useful in performing and streamlining needle localization and stereotactic procedures. The time necessary for a patient to remain still and in compression for these procedures is greatly reduced when using digital imaging.

Computer Aided Detection (CAD): The false-negative rate for mammography has been reported to be between 10% and 30% (Ganott et. al 1999, Morton et al 2006 and James et al. 2004). However, Sensitivity can be improved further by 5% to 15% by inter rater reliability, when two radiologists are used rather than one (Destounis et. al 2004, Morton et al. 2006) which aids in costs expenses incurred from double reading. CAD systems have proven to be quite sensitive in detecting breast cancers on screening mammograms. Studies have shown that CAD correctly highlight 98% of microcalcifications, 86% to 88% of masses, and 90% of all cancers (Castellino et al. 2000, James et al. 2004). The detection rates tend to increase with the level of mammographic suspicion (Baum et al. 2002). Specificity, however, proves to be a problem with CAD. A retrospective review by a panel of 5 radiologists of the prior mammograms of these biopsy-proven breast cancer cases showed that 286 (67%) of 427 were visible and that 115 (27%) of 427 of these warranted recalls. CAD flagged 89 (77%) of these 115 cases. To recapitulate, numerous studies have demonstrated the positive effects of CAD on breast cancer detection rates in screening mammography (Ganott et. al 1999, Castellino et al. 2000, Destounis et. al 2004, James et al. 2004, Morton et al 2006). CAD does not seem to significantly increase recall rates, although the algorithms allow for many false-positive prompts. CAD has the greatest potential impact on finding microcalcifications, particularly in dense breasts, that might otherwise be overlooked by radiologists. CAD can also have false-negative results; therefore, the absence of CAD detection of an otherwise suspicious mammographic finding should not prevent a diagnostic workup.

Ultrasonography (USG): Breast ultrasound is often used as a supplementary tool in assessing impalpable breast abnormalities and mammographically occult lesions. Its results are strongly dependent on the examiner's interpretation. It differentiates cystic from solid lesions; benign and malignant breast neoplasm in women aged 40 years or younger when mammography is less sensitive due to dense breasts. The sensitivity of detecting cancer is reported as 65% and 92% for cystic masses (Kailash et al. 2008). However, USG screening of asymptomatic women gives high rates of both false positive and false negative outcomes and difficulty in detecting microcalcification in ductal carcinoma in situ (Rankin 2000; Gordon 2002). Generally, biopsies, which are at the end of today's breast cancer detection clinical work flow, show a large number of false-positive cases for the established imaging modalities. (Christiansen et al. 2000, Hubbard et al. 2011). However, the color doppler help to assess the aggressiveness of lesion by demonstrating the increased vascularity and assessing the lymphnodes. The use of contrast-enhanced power Doppler sonography has managed to detect vessels in up to 95% of malignant tumors.

Fine Needle Aspiration Cytology (FNAC): Is considered as the gold standard method, cost-effective and useful for mass lesions (Giard et al. 1992). It has a sensitivity and specificity of > 90% and > 65%, respectively. The positive predictive value was reported to be > 99% (Kocjan 2008) depending on the skill of the person performing the aspiration and expertise of the cytopathologist. Sometimes the problematic cells are missed, resulting in a false negative result. Further, FNAC cannot reliably predict the invasion of a tumor (Tse et al. 2010).

Core Needle Biopsy (CNB): Is a percutaneous procedure that involves removing a small amount of breast tissue using a hollow "core" needle (DeAngelis et al. 1998; Kocjan 2008). It allows more accurate assessment of breast mass or non-mass lesions than FNAC. It is reported that CNB has a high specificity of 99% (de Waal et al. 2006) and it improves the preoperative diagnosis more often than repeat FNAC (78.0% vs. 54.8%) (Kooistra et al. 2009). Limitation of CNB is difficulty in assessing deeply seated lump within the breast.

Breast MR Imaging

Magnetic Resonance Imaging (MRI): Is a recent method that is used for diagnosis and monitoring the response of therapeutic response of breast cancer patients. Where, both x-ray mammogram and USG give low specificity and also has limitations in identifying lesions in dense breast or microcalcification. In this regard, interest is focused on breast MRI and its potential in clinical setting has been reported (Rankin 2000; Goscin et al. 2001; Sardanelli 2004; Jagannathan et al. 2005; Deurloo et al 2005; Von Goethem et al 2006; Jagannathan et al. 2009; Kuhl 2007a; Kuhl 2007b; Partridge et al. 2008; Sharma et al. 2010).

Dynamic Contrast Enhanced MRI (DCE-MRI): Helps in assessing the functional and morphologic properties of a tumor (like angiogenesis, size etc.) (Stomper et al. 1997; Kuhl et al. 2006; Kuhl 2007a; Warner et al. 2008; Huang et al. 2010). The method is helpful to improve the ability to differentiate malignant from benign breast lesions in high-risk women (Komatsu et al. 2005; Warren et al. 2006). It is useful for delineation of multifocal breast lesions with high sensitivity (93 - 99%) but low specificity (37 - 85%) (Warren et al. 2006)). The high sensitivity of DCE-MRI is suitable for diagnosis, but the limitation of its lower specificity is a major drawback (Boetes et al. 1994; Saslow et al. 2007). Further the specificity might be achieved by combining both the morphological features and the enhancement kinetics information (Degani et al. 1997; Liberman et al. 2002). Kuhl and Goto et al. (2005a) and Goto et al. (2007) compared the dynamic enhancement patterns and morphological features of enhancing lesions. Other studies have suggested the improved diagnostic accuracy of breast MRI (Degani et al. 1997; Liberman et al. 2002, Schnall et al. 2006) by a combination of both the dynamic uptake and morphological features. It was shown that increased predictive value could be obtained when integration of both morphology and contrast uptake dynamics is taken in to consideration (Schnall et al. 2006).

MR Elastography (MRE): Is a novel non-invasive technique to measure the spatial stiffness of soft tissues. The routine breast screening as malignant masses are known to be stiffer than benign lesions and normal breast tissue (Krouskop et al. 1998, Samani et al. 2007), it lacks great sensitivity and specificity as a diagnostic test. MRE is well suited for breast cancer diagnosis and staging as a means to quantify the properties currently assessed by manual palpation. Some studies have documented the differentiation between normal, malignant and benign tumors (Lorenzen et al. 2002; Xydeas et al. 2005). This may overcome the limitations of manual palpation and increase the DCE-MRI specificity as well (Sinkus et al. 2000; Manduca et al. 2001; Oliphant et al. 2001; Sinkus et al. 2007). While the initial results are encouraging, the most significant limitation for MRE in breast cancer is spatial resolution and detection of small focal lesions.

***Diffusion Weighted Imaging*:** Considering the low specificity of DCE-MRI, diffusion-weighted imaging (DWI) based on measurement of water diffusion properties of tissues has been explored by many researchers (Marini et al. 2007; Luo; et al. 2007; Baron et al. 2010; Malayeri et al. 2011; Petralia et al. 2011; Iima et al. 2011; Malayeri et al. 2011; Hirano et al. 2012). Englander et al. were the first to report DWI of the breast (Englander et al. 1997). DWI is valuable in diagnosis and assessing the therapeutic response of breast tumors (Guo et al. 2002; Kuroki et al. 2004; Woodhams et al. 2005a; Woodhams et al. 2005b; Rubesova et al. 2006; Manton et al 2006; Luo et al. 2007; Yankeelov et al 2007; Kuroki et al. 2008; Woodhams et al. 2009; Sharma et al 2009; Siegmann et al. 2011; McLaughlin et al. 2011; Rahbar et al. 2011; Iacconi et al. 2011; Pereira et al. 2011; Sonmez et al. 2011; Kawamura et al. 2011; Belli et al. 2011; Jensen et al. 2011; Shin et al 2011; Park et al. 2012; Wu et al. 2012; Türkbey et al. 2012; Shin et al. 2012). Studies have shown that apparent diffusion coefficient (ADC) was lower in malignant tumors compared to normal and benign breast tissues (Luo et al. 2007; Pereira et al. 2011, Sharma et al. 2016). Kul et al. (2011) have reported a higher sensitivity of 97.9% with a lower specificity of 75.7% using DCE- MRI, while DWI gave a lower sensitivity and a higher specificity of 91.5% and 86.5% in the characterization of malignant and benign breast lesions. For characterization of breast lesions into malignant and benign using ADC values, several groups have reported a sensitivity and specificity of 93% and 88%, respectively (Guo et al. 2002; Jin G et al. 2010). Sharma et al also reported the role of DWI for the differentiation of viable and necrotic areas of breast cancer and its potential utility to guide voxel positioning for MRS in the absence of dynamic contrast-enhanced MRI data (Sharma et al. 2012). The usefulness of ADC values to differentiate non-responders from responders as early as the first cycle of NACT compared to the tumor diameter (Sharma et al. 2009, Agrawal et al. 2017).

Apart from the above imaging methods, *in vivo*, magnetic resonance spectroscopy (MRS) on the other hand provides biochemical information of tissues. Phosphorus (^{31}P) and proton (^{1}H) are the most widely used nuclei in clinical MRS studies of cancer, providing biochemical information at the metabolite level. The potential of MRS for studying cellular metabolism *in*

vivo was first demonstrated using ^{31}P spectra acquired from animal tissues (Hoult et al. 1974). ^{31}P MRS has been used for characterization and therapeutic assessment of breast tumors (Glaholm et. al 1989; Redmond et al. 1991; Leach et al. 1998; Ronen et al. 2001). Although ^{31}P MRS studies demonstrated promising results, its lower MR sensitivity and requirements of special hardware limit its use in clinical settings. Further, Park et al. reported that ^{31}P MRS studies were not helpful for demonstrating differential diagnosis between malignant and benign breast lesions (Park et al. 2001).

Magnetic Resonance Spectroscopy: Thus, *in vivo* MRS studies on breast mostly use ^{1}H nucleus and these are of two types: (i) single-voxel spectroscopy (SVS), and (ii) multi-voxel spectroscopy, also known as magnetic resonance spectroscopic imaging (MRSI). SVS method acquires the signal from a single volume of interest, while MRSI acquires spectrum from multiple voxels simultaneously. MRSI has the ability to assess multiple lesions and normal tissues simultaneously, as well as to distinguish lesion borders and infiltration into the surrounding tissues (Katz-Brull et al. 2002; Bolan et al. 2003; Baik et al. 2006; Baik et al. 2005; Baek et al. 2008; Danishad et al. 2010). SVS has been shown to be robust in the estimation of tCho concentration in differentiating various breast tissues (Katz-Brull et al 2002; Bolan et al. 2003; Baik et al. 2006; Baek et al. 2008). In order to characterize different breast tissues (diseased and normal) two important parameters have been measured from the *in vivo* ^{1}H MRS: (i) water to fat (W-F) ratio, and (ii) total choline (tCho) concentration. Sijens et al. (1988) were the first to report breast MRS using W-F ratio demonstrating higher W-F ratio in breast cancer compared to normal breast tissues. Later several studies reported that malignant breast tissues show increased water signal with a high W-F ratio as compared to normal breast tissues (Jagannathan et al. 1998; Jagannathan et al. 1999; Kumar et al. 2006).

Later ^{1}H MRS studies showed the observation of tCho peak in malignant breast lesions and reported its potential to differentiate malignant from benign tissues (Jagannathan et al. 1998; Roebuck et al. 1998; Jagannathan et al. 1999; Cecil et al. 2001; Yeung et al. 2001; Jagannathan et al. 2001; Katz-Brull et al. 2002; Gary et al. 2007; Stanwell and Mountford, 2007; Sharma et al. 2008; Sardanelli et al. 2008). In differentiating malignant from benign lesions (in younger patients), a sensitivity of 100% and a specificity of 89% to 100% were reported using MRS (Roebuck et al. 1998; Cecil et al. 2001; Yeung et al. 2001; Shrama et al. 20011). Several groups based on observation of presence/absence of tCho resonance reported 83% sensitivity with the specificity of 85% in detecting cancer and indicated that these values could be as high as 92% (Katz-Brull et al. 2002; Haddadin et al. 2009).

Potential of tCho SNR (signal-to-noise ratio) was also reported for differential diagnosis of malignant and normal breast tissues and for assessing the response to chemotherapy (Hu et al. 2005; Bartella et al. 2006; Danishad et al. 2010). Studies have documented that the application of *in vivo* MRS in a clinical setting might increase the specificity of MRI (Meisamy et al. 2005; Mountford et al. 2009). However, with the advancement in hardware, coil technology and improved pulse sequences for simultaneous suppression of both water and fat resonances, the tCho peak has been observed frequently in benign lesions, in normal breast tissue of volunteers as well as in the breast of lactating women (Roebuck et al. 1998; Jagannathan et al. 1998; Kvistad et al.1999; Jagannathan et al. 2001; Kim et al. 2003; Jacobs et al. 2004; Stanwell et al. 2005; Baek et al. 2008; Sah et al. 2009, 2010 and 2012, Sah et al. 2015). These findings indicated that the qualitative or semi-quantitative assessment of tCho is not sufficient for the differentiation of malignant, benign and normal breast tissues.

Thus, there is a need for quantitative estimation of tCho concentration to differentiate various lesion types and the normal breast tissues. Different research groups have reported the absolute concentration of tCho in the range of 0.7 - 21.2 mmol/kg in malignant tumors (Roebuck et al. 1998; Meisamy et al. 2005; Baik et al. 2006, Sah et al. 2012a and 2012b). The changes in the concentration of tCho for monitoring the response of tumors to chemotherapeutic agents have also been reported by various research groups (Meisamy et al. 2004; Tan et al. 2006; Baek et al. 2008; Sah et al. 2009; Baek et al. 2009; Sharma et al. 2010; Sah et al. 2010; Tozaki et al. 2010b, Sharma et al. 2018). Tozaki et al. (2008 and 2010b) reported their findings based on tCho integral and reported either absence or reduction in the tCho concentration as a result of response to treatment. Reduction in tCho concentration has been shown to occur as early as twenty four hours after the first cycle of chemotherapy (Meisamy et al. 2004).

Molecular Imaging

Positron Emission Tomography: provides physiology in addition to anatomical information. The administered Fluro Deoxy Glucose (FDG) is transported through glucose transporter into cells Converted into FDG 6 Phosphate which are Trapped within the cell and decays to emit positron (positive electron). It potential application lies in detection of breast malignancy – in dense breasts, implanted breasts, occult primary, nodal metastases – axillary and inframammary, Systemic metastases, response to chemotherapy (Tozaki et al. 2008 and 2010a). However, it is Less sensitive for tumors < 1cm, slowly growing tumors.

Positron Emission Mammography*:* It is considered small less expensive PET unit specially designed for breast and is more sensitive and can detect tumors up to 12mm. The compression can be applied and attached to

mammographic unit. It helps in prediction of early response to chemotherapeutic agents.

Scintimammography: Scintimammography involves the use of non specific tumors imaging radionuclides as well as other agents such Indium labeled somatostanin analysis and monoclonal antibodies in diagnosis and staging of breast cancer. The most commonly used radionuclides are Tl-201, Tc99m Sestabini, Tc99m tetrofosmin and bone imaging agent Tc 99m methylene diphosphonate.

Under Research

Optical Imaging: Optical imaging is considered as a noninvasive, in vivo imaging and use for quantification of oxy, deoxy hemoglobin and contrast agents - thereby assessing the tumor angiogenesis and hypoxia. This imaging tool does not use ionizing radiation. The Indo Cyanine Green (ICG), an intravenous contrast agent extravasates through tumor vessels of high permeability is detected with near infrared part of spectrum. It can be combined with other imaging modalities - USG, MRI and PET (Ntziachristos et al. 2001). During the last 20 years, tremendous amount of work has been carried out on in vivo optical imaging of the female breast. Starting from attempts to obtain high-contrast images of breast carcinomas by a noninvasive and comparably cheap method, the focus of research moved more and more to the development of methods suited to quantitatively measure the functional parameters of breast tissue and to understand the origin of contrast in near-infrared images of diseased as well as healthy breast tissue Currently, sensitivity and specificity of optical mammography are likely too low for its application as a screening tool. More importantly, the poor spatial resolution of diffuse optical imaging prevents early detection of breast cancer, which is a main aim of screening (Grosenick et. al. 2018).

T Scan: It measures low level bioelectric currents to produce real images of electrical impedance properties of breast tissues. No ionizing radiation or compression of breast is used. One volt of continuous electricity is transmitted into body through electrode patches attached to the arm and measured with probe placed on breast. Tumors conduct electricity differently than healthy tissues and appear as bright white spots.

Summary

Mammography is the best screening modality for asymptomatic women and the initial imaging modality for symptomatic women >30 years of age. Full-field digital mammography is superior to standard mammography in women under 50 years of age and in those with dense breasts and may likely increase its sensitivity and specificity. USG is used for characterization of the mammographic abnormality and for primary imaging of young women <30 years. Color power doppler has adjunct value to differentiate the benign from malignant lesions. Contrast enhancement may further refine its current status. MR elastography need further studies to establish their roles as is limited by spatial resolution.

Contrast enhanced MRI is so far the most sensitive technology for the diagnosis of malignancy at the expense of reduced specificity. Its scopes are further expanding to include staging of tumor and detection of recurrences. The addition of MR Spectroscopy can improve its specificity. Molecular imaging can be useful in a select group of patients like those with suspected distant metastases, to evaluate loco regional extent, to detect the recurrence and monitor response to therapy.

Recent Advancement and Future Directions

Optical imaging and T Scan currently under research have potential to emerge as an adjunct to the existing technologies. The ideal modality for breast imaging in future, should lead to early detection of cancer, should be free from adverse effects and should be cost effective. It should be capable of delineating the benign from the malignant masses, thereby avoiding unnecessary biopsies and further help in assessing the response of chemotherapeutic agents. This information can provide targets for new drug development and understanding of breast tumor heterogeneity. Technologies for imaging the breast continue to advance, however cost issues may be limiting factor for their widespread application in the clinical setting.

Authors Disclosures: The authors have no conflict of interest to declare.

REFERENCES

1. Agarwal K, Sharma U, Sah RG, Mathur S, Hari S, Seenu V, Parshad R, Jagannathan NR. Pre-operative assessment of residual disease in locally advanced breast cancer patients: A sequential study by quantitative diffusion weighted MRI as a function of therapy. Magn Reson Imaging, 2017; 42: 88-94.
2. Baek HM, Chen JH, Nie K, Yu HJ, Bahri S, Mehta RS, Nalcioglu O and Su MY (2009). Predicting pathologic response to neoadjuvant chemotherapy in breast cancer by using MR imaging and quantitative ^{1}H MR spectroscopy. *Radiology*, 251: 653-62.
3. Baek HM, Chen JH, Yu HJ, Mehta R, Nalcioglu O, Su MY (2008). Detection of choline signal in human breast lesions with chemical-shift imaging. *J Magn Reson Imaging*, 27: 1114-21.
4. Baek HM, Chen JH, Nalcioglu O, Su MY (2008). Proton MR spectroscopy for monitoring early treatment response of breast cancer to neo-adjuvant chemotherapy. *Ann Oncol.*, 19: 1022-4.
5. Baik HM, Su MY, Yu HJ, Mehta R, Nalcioglu O (2006). Quantification of choline containing compounds in malignant breast tumors by ^{1}H MR spectroscopy using water as an internal reference at 1.5 T. *MAGMA*, 19: 96-104.
6. Baik H-M, Su M-Y, Yu HJ, Nalcioglu O (2005). Proton chemical shift imaging for monitoring early

treatment response of breast cancer to neoadjuvant chemotherapy. *Proc Intl Soc Mag reson Med.,* 13: 1879.
7. Baron P, Dorrius MD, Kappert P, Oudkerk M, Sijens PE (2010). Diffusion-weighted imaging of normal fibroglandular breast tissue: influence of microperfusion and fat suppression technique on the apparent diffusion coefficient. *NMR Biomed.,* 23: 399-405.
8. Bartella L, Morris EA, Dershaw DD, Liberman L, Thakur SB, Moskowitz C, Guido J, Huang W (2006). Proton MR spectroscopy with choline peak as malignancy marker improves positive predictive value for breast cancer diagnosis: preliminary study. *Radiology,* 239: 686-92.
9. Baum F, Fischer U, Obenauer S, et al (2002). Computer-aided detection in direct digital full-field mammography: initial results. Eur Radiol, 12: 3015-3017.
10. Belli P, Costantini M, Ierardi C, Bufi E, Amato D, Mule' A, Nardone L, Terribile D, Bonomo L (2011). Diffusion-weighted imaging in evaluating the response to neoadjuvant breast cancer treatment. *Breast J.,* 17: 610-9. (Epub).
11. Boetes C, Barentsz JO, Mus RD, van der Sluis RF, van Erning LJ, Hendriks JH, Holland R, Ruys SH (1994). MR characterization of suspicious breast lesions with a gadolinium-enhanced Turbo FLASH subtraction technique. *Radiology,* 193: 777-81.
12. Bolan PJ, Meisamy S, Baker EH, Lin J, Emory T, Nelson M, Everson LI, Yee D, Garwood M (2003). *In vivo* quantification of choline compounds in the breast with ^{1}H MR Spectroscopy. *Magn Reson Med.,* 50: 1134-43.
13. C. L. Christiansen et al (2000), Predicting the cumulative risk of false-positive mammograms, J. Natl. Cancer Inst., 92(20): 1657–1666.
14. C.K., Schild, H.H. and Morakkabati, N. (2005). Dynamic bilateral contrast-enhanced MR imaging of the breast: trade-off between Spatial and temporal resolution. Radiology, 236: 789-800.
15. Castellino RA, Roehrig J, Zhang W (2000). Improved computer-aided detection (CAD) algorithms for screening mammography. Radiology, 217: 400.
16. Cecil KM, Schnall MD, Siegelman ES, Lenkinski RE (2001). The evaluation of human breast lesions with magnetic resonance imaging and proton magnetic resonance spectroscopy. *Breast Cancer Res Treat.,* 6: 45-54.
17. Costantini M, Belli P, Rinaldi P, Bufi E, Giardina G, Franceschini G, Petrone G, Bonomo L (2010). Diffusion-weighted imaging in breast cancer: relationship between apparent diffusion coefficient and tumour aggressiveness. *Clin Radiol.,* 65: 1005-12.
18. Danishad K. A, Sharma U, Sah RG. Parshad R, Seenu V and Jagannathan NR (2010). Assessment of therapeutic response of locally advanced breast cancer (LABC) patients undergoing neoadjuvant chemotherapy (NACT) monitored using sequential magnetic resonance spectroscopic imaging (MRSI). *NMR Biomed.,* 23: 233-41.
19. de Waal JC, Prechtel K, Weitz J, Staufer F, Pankratz-Hauer M, Nerlich A (2006). Scope and limitations of diagnostics in breast disease--focussing on large core biopsy. *Ultraschall Med.,* 27: 456-61.
20. DeAngelis GA, Fajardo LL, Harvey JA, Hatwal N, Moran RE (1998). Percutaneous breast biopsy for nonpalpable lesions. *Breast Dis*., 10: 67-81.
21. Degani, H., Gusis, V., Weinstein, D. et al. (1997). Mapping pathophysiological features of breast tumors by MRI at high spatial resolution. Nat. Med., 3: 780–2.
22. Destounis SV, DiNitto P, Logan-Young W, et al (2004). Can computer-aided detection with double reading of screening mammograms decrease the falsenegative rate? Initial experience. Radiology, 232: 578-584.
23. Deurloo EE, Peterse JL, Rutgers EJ, Besnard AP, Muller SH, Gilhuijs KG (2005). Additional breast lesions in patients eligible for breast-conserving therapy by MRI: Impact on pre-operative management and potential benefit of computerized analysis. *Eur J Cancer,* 41: 1393-401.
24. E. D. Pisano et al. (2005), "Diagnostic performance of digital versus film mammography for breast-cancer screening," N. Engl. J. Med., 353(17): 1773–1783.
25. Englander SA, Uluğ AM, Brem R, Glickson JD, van Zijl PC (1997). Diffusion imaging of human breast. *NMR Biomed.,* 10: 348-52.
26. Ganott MA, Harris KM, Klaman HM, et al (1999). Analysis of false-negative cancer cases identified with a mammography audit. Breast J., 5: 166-175.
27. Gary MT, David KY, Ann DK, Humairah S. Cheung, Wei-Tse Yang (2007). *In vivo* magnetic resonance spectroscopy of breast lesions: an update. *Breast Cancer Res Treat.,* 104: 249-55.
28. Giard RW, Hermans J (1992). The value of aspiration cytologic examination of the breast. A statistical review of the medical literature. *Cancer,* 69: 2104-10.
29. Glaholm J, Leach MO, Collins DJ, Mansi J, Sharp JC, Madden A, Smith IE, McCready VR (1989). In-vivo ^{31}P magnetic resonance spectroscopy for monitoring treatment response in breast cancer. *Lancet,* 1: 1326-7.
30. Gordon PB (2002). Ultrasound for breasts cancer screening and staging. *Radiol. Clin. North Am.,* 40: 431–41.
31. Goscin CP, Berman CG, Clark RA (2001). Magnetic resonance imaging of the breast. Cancer Control, 8: 399-406.
32. Goto, M., Ito H., Akazawa, K. et al. (2007). Diagnosis of breast tumors by contrast-enhanced MR imaging: comparison between the diagnostic performance of dynamic enhancement patterns and

morphologic features. J. Magn. Reson. Imaging, 25: 104–12.
33. Grosenick D, Wabnitz H, Macdonald R (2018). Diffuse near-infrared imaging of tissue with picosecond time resolution. Biomed Tech (Berl). doi: 10.1515/bmt-2017-0067.
34. Guo Y, Cai YQ, Cai ZL, Gao YG, An NY, Ma L, Mahankali S, Gao JH (2002). Differentiation of clinically benign and malignant breast lesions using diffusion-weighted imaging. *J. Magn. Reson. Imaging*, 16: 172-8.
35. Haddadin IS, McIntosh A, Meisamy S, Corum C, Styczynski Snyder AL, Powell NJ, Nelson MT, Yee D, Garwood M, Bolan PJ (2009). Metabolite quantification and high-field MRS in breast cancer. *NMR Biomed.*, 22: 65-6.
36. Hirano M, Satake H, Ishigaki S, Ikeda M, Kawai H, Naganawa S (2012). Diffusion-weighted imaging of breast masses: comparison of diagnostic performance using various apparent diffusion coefficient parameters. *AJR Am J Roentgenol*., 198: 717-22.
37. Hoult DI, Busby SJW, Gadian DG, Radda GK, Richards RE, Seeley PJ (1974). Observation of tissue metabolites using ^{31}P nuclear magnetic resonance. *Nature*, 252: 285-7.
38. Hu J, Vartanian SA, Xuan Y, Latif Z, Soulen RL (2005). An improved 1H magnetic resonance spectroscopic imaging technique for the human breast. Proc Intl Soc Mag Reson Med., 13: 134.
39. Huang CF, Chiou SY, Wu MF, Tu HT, Liu WS, Chuang JC (2010). Apparent diffusion coefficients for evaluation of the response of brain tumors treated by Gamma Knife surgery. *Neurosurg.*, 113: 97-104.
40. Iacconi C, Giannelli M (2011). Can diffusion-weighted MR imaging be used as a biomarker for predicting response to neoadjuvant chemotherapy in patients with locally advanced breast cancer? *Radiology*, 259: 303-4.
41. Iima M, Le Bihan D, Okumura R, Okada T, Fujimoto K, Kanao S, Tanaka S, Fujimoto M, Sakashita H, Togashi K (2011). Apparent diffusion coefficient as an MR imaging biomarker of low-risk ductal carcinoma in situ: a pilot study. *Radiology*, 260: 364-72.
42. Jacobs MA, Barker PB, Bottomley PA, Bhujwalla Z, Bluemke DA (2004). Proton magnetic resonance spectroscopic imaging of human breast cancer: a preliminary study. *J Magn Reson Imaging*, 19: 68-75.
43. Jagannathan NR (2005). Recent advances in MR imaging and spectroscopy. New Delhi, Jaypee Brothers.
44. Jagannathan NR, Kumar M, Seenu V, Coshic O, Dwivedi SN, Julka PK, Srivastava A, Rath GK (2001). Evaluation of total choline from in-vivo volume localized proton MR spectroscopy and its response to neoadjuvant chemotherapy in locally advanced breast cancer. *Br J Cancer*, 84: 1016-22.
45. Jagannathan NR, Singh M, Govindaraju V, Raghunathan P, Coshic O, Julka PK and Rath GK (1998). Volume localized *in vivo* proton MR spectroscopy of breast carcinoma: Variation of W/F ratio in patients receiving chemotherapy. *NMR Biomed.*, 11: 414-22.
46. Jagannathan NR. (ed) 2009. Breast MR. *NMR Biomed.*, 22: 1-127.
47. Jagannathan, NR, Kumar, M, Raghunathan, P. Coshic, O, Julka, PK, Rath, GK (1999). Assessment of the therapeutic response of human breast carcinoma using *in vivo* volume localized proton magnetic resonance spectroscopy. *Curr. Sci.*, 76: 777–82.
48. James JJ (2004). The current status of digital mammography. Clin Radiol, 59: 1-10.
49. Jensen LR, Garzon B, Heldahl MG, Bathen TF, Lundgren S, Gribbestad IS (2011). Diffusion-weighted and dynamic contrast-enhanced MRI in evaluation of early treatment effects during neoadjuvant chemotherapy in breast cancer patients. *J Magn Reson Imaging*, 34: 1099-109. (Epub).
50. Jin G, An N, Jacobs MA, Li K (2010). The role of parallel diffusion-weighted imaging and apparent diffusion coefficient (ADC) map values for evaluating breast lesions: preliminary results. *Acad Radiol*., 17: 456-63.
51. Kailash S, Tariq A, Ghanshyam DG (2008). The accuracy of Ultrasound in characterization of palpable breast lumps. *JK Science*, 10: 186-88.
52. Katz-Brull R, Lavin PT, Lenkinski RE (2002). Clinical utility of proton magnetic resonance spectroscopy in characterizing breast lesions. *J Natl Cancer Inst.*, 94: 1197-203.
53. Kawamura M, Satake H, Ishigaki S, Nishio A, Sawaki M, Naganawa S (2011). Early prediction of response to neoadjuvant chemotherapy for locally advanced breast cancer using MRI. *Nagoya J Med Sci.*, 73: 147-56.
54. Kim JK, Park SH, Lee HM, Lee YH, Sung NK, Chung DS, Kim OD (2003). *In vivo* ^{1}H-MRS evaluation of malignant and benign breast diseases. *Breast*, 12: 179-82.
55. Kocjan G (2008). Needle aspiration cytology of the breast: current perspective on the role in diagnosis and management. *Acta Med Croatica*, 62: 391-401.
56. Komatsu S, Lee CJ, Ichikawa D, Hamashima T, Morofuji N, Shirono K, Hosokawa Y, Okabe H, Kurioka H, Yamagishi H, Oka T (2005). Predictive value of the time-intensity curves on dynamic contrast-enhanced magnetic resonance imaging for lymphatic spreading in breast cancer. *Surg Today*, 35: 720-4.
57. Kooistra B, Wauters C, Strobbe L (2009). Indeterminate breast fine-needle aspiration: repeat aspiration or core needle biopsy? *Ann Surg Oncol.*, 16: 28-4.
58. Krouskop TA, Wheeler TM, Kallel F, Garra BS, Hall T (1998). Elastic moduli of breast and prostate

tissues under compression. Ultrason Imaging, 20: 260–274.
59. Kuhl C (2007a). The Current Status of breast MR imaging. Part I. Choice of technique, image interpretation, diagnostic accuracy and transfer to clinical practice. *Radiology*, 244: 356-78.
60. Kuhl CK (2007b). Current status of breast MR imaging. II. Clinical applications. *Radiology*, 244: 672-691.
61. Kuhl CK, Jost P, Morakkabati N, Zivanovic O, Schild HH, Gieseke J (2006). Contrast-enhanced MR imaging of the breast at 3.0 and 1.5 T in the same patients: initial experience. *Radiology*, 239: 666-76.
62. Kul S, Cansu A, Alhan E, Dinc H, Gunes G, Reis A (2011). Contribution of diffusion-weighted imaging to dynamic contrast-enhanced MRI in the characterization of breast tumors. *AJR Am J Roentgenol.*, 196: 210-7.
63. Kumar M, Jagannathan NR, Seenu V, Dwivedi SN, Julka PK, Rath GK (2006). Monitoring the therapeutic response of locally advanced breast cancer patients: sequential *in vivo* proton MR spectroscopy study. *J Magn Reson Imaging*, 24: 325-32.
64. Kuroki Y, Nasu K (2008). Advances in breast MRI: diffusion-weighted imaging of the breast. *Breast Cancer*, 15: 212-7.
65. Kuroki Y, Nasu K, Kuroki S, Murakami K, Hayashi T, Sekiguchi R, Nawano S (2004). Diffusion-weighted imaging of breast cancer with the sensitivity encoding technique: analysis of the apparent diffusion coefficient value. *Magn. Reson. Med. Sci.*, 3: 79-85.
66. Kvistad KA, Bakken IJ, Gribbestad IS, Ehrnholm B, Lundgren S, Fjosne HE, Haraldseth O (1999). Characterization of neoplastic and normal human breast tissues with *in vivo* ^{1}H MR Spectroscopy. *J Magn Reson Imaging*, 10: 159-64.
67. Leach MO, Verrill M, Glaholm J, Smith TA, Collins DJ, Payne GS, Sharp JC, Ronen SM, McCready VR, Powles TJ, Smith IE (1998). Measurements of human breast cancer using magnetic resonance spectroscopy: a review of clinical measurements and a report of localized ^{31}P measurements of response to treatment. *NMR Biomed.*, 11: 314-40.
68. Liberman, L., Morris, E.A., Lee, M.J. et al. (2002). Breast lesions detected on MR imaging: features and positive predictive value. AJR Am. J. Roentgenol., 179: 171–8.
69. Lorenzen, J., Sinkus, R., Lorenzen, M. et al. (2002). MR elastography of the breast: preliminary clinical results. Rofo., 174: 830–4.
70. Luo JD, Liu YY, Zhang XL, Shi LC (2007). Application of diffusion weighted magnetic resonance imaging to differential diagnosis of breast diseases. *Ai Zheng*, 26: 168-71.
71. Malayeri AA, El Khouli RH, Zaheer A, Jacobs MA, Corona-Villalobos CP, Kamel IR, Macura KJ (2011). Principles and applications of diffusion-weighted imaging in cancer detection, staging, and treatment follow-up. *Radiographics*, 31: 1773-91. (Review).
72. Manduca, A., Oliphant, T.E., Dresner, M.A. et al. (2001). Magnetic resonance elastography: non-invasive mapping of tissue elasticity. Med. Image Anal., 5: 237-54.
73. Manton DJ, Chaturvedi A, Hubbard A, Lind MJ, Lowry M, Maraveyas A, Pickles MD, Tozer DJ, Turnbull LW (2006). Neoadjuvant chemotherapy in breast cancer: early response prediction with quantitative MR imaging and spectroscopy. *Br. J. Cancer*, 94: 427-35.
74. McLaughlin R, Hylton N (2011). MRI in breast cancer therapy monitoring. *NMR Biomed.*, 24: 712-20. (Review).
75. Meisamy S, Bolan PJ, Baker EH, Bliss RL, Gulbahce E, Everson LI, Nelson MT, Emory TH, Tuttle TM, Yee D, Garwood M (2004). Neoadjuvant chemotherapy of locally advanced breast cancer: predicting response with *in vivo* ^{1}H MR spectroscopy: a pilot study at 4 T. *Radiology*, 233: 424-31.
76. Meisamy S, Bolan PJ, Baker EH, Pollema MG, Le CT, Kelcz F, Lechner MC, Luikens BA, Carlson RA, Brandt KR, Amrami KK, Nelson MT, Everson LI, Emory TH, Tuttle TM, Yee D, Garwood M (2005). Adding in-vivo quantitative ^{1}H MR Spectroscopy to improve diagnostic accuracy of breast MR imaging: preliminary results of observer performance study at 4.0 T. *Radiology*, 236: 465-75.
77. Morton MJ, Whaley DH, Brandt KR, et al (2006). Screening mammograms: interpretation with computer-aided detection: prospective evaluation. Radiology, 2006; 239: 375-383.
78. Mountford C, Ramadan S, Stanwell P, Malycha P (2009). Proton MRS of the breast in the clinical setting. *NMR Biomed.*, 22: 54-64.
79. Ntziachristos V, Chance B (2001). Probing physiology and molecular function using optical imaging: applications to breast cancer. Breast Cancer Res., 3(1): 41-6.
80. Oeffinger KC, Fontham ET, Etzioni R et al (2015). Breast cancer screening for women at average risk: 2015 guideline update from the american cancer society. JAMA, 314: 1599-1614.
81. Oliphant, T.E., Manduca, A., Ehman, R.L. et al. (2001). Complex-valued stiffness reconstruction for magnetic resonance elastography by algebraic inversion of the differential equation. Magn. Reson. Med., 45: 299-310.
82. Park JM, Park JH (2001). Human in-vivo ^{31}P MR spectroscopy of benign and malignant breast tumors. *Korean J Radiol.*, 2: 80-6.
83. Park SH, Moon WK, Cho N, Chang JM, Im SA, Park IA, Kang KW, Han W, Noh DY (2012). Comparison of diffusion-weighted MR imaging and FDG PET/CT to predict pathological complete response to neoadjuvant chemotherapy in patients with breast cancer. *Eur Radiol.*, 22: 18-25.

84. Partridge SC (2008). Future applications and innovations of clinical breast magnetic resonance imaging. *Top Magn Reson Imaging*, 19: 171-6.
85. Pereira FP, Martins G, Carvalhaes de Oliveira Rde V (2011). Diffusion magnetic resonance imaging of the breast. *Magn Reson Imaging Clin N Am*., 19: 95-110.
86. Petralia G, Bonello L, Priolo F, Summers P, Bellomi M (2011). Breast MR with special focus on DW-MRI and DCE-MRI. *Cancer Imaging*, 11: 76-90.
87. R.A. Hubbard et al. (2011) Cumulative probability of false-positive recall or biopsy recommendation after 10 years of screening mammography: a cohort study, Ann. Intern. Med., 155(8): 481-492.
88. Rahbar H, Partridge SC, Eby PR, Demartini WB, Gutierrez RL, Peacock S, Lehman CD (2011). Characterization of ductal carcinoma in situ on diffusion weighted breast MRI. *Eur Radiol.*, 21: 2011-9.
89. Rankin SC (2000). MRI of the breast. *Br J Radiol.*, 73: 806-18.
90. Redmond OM, Stack JP, O'Connor NG, Codd MB, Ennis JT (1991). *In vivo* phosphorus-31 magnetic resonance spectroscopy of normal and pathological breast tissues. *Br J Radiol.*, 64: 210-6.
91. Roebuck JR, Cecil KM, Schnall MD, Lenkinski RE (1998). Human breast lesions: Human breast lesions: characterization with proton MR spectroscopy. *Radiology*, 209: 269-75.
92. Ronen SM, Leach MO (2001). Imaging biochemistry: applications to breast cancer. Breast *Cancer Res*., 3: 36-40.
93. Rubesova E, Grell AS, De Maertelaer V, Metens T, Chao SL, Lemort M (2006). Quantitative diffusion imaging in breast cancer: a clinical prospective study. *J Magn Reson Imaging*, 24: 319-24.
94. Sah RG, Agarwal K, Sharma U, Parshad R, Seenu V, Jagannathan NR (2015). Characterization of malignant breast tissue of breast cancer patients and the normal breast tissue of healthy lactating women volunteers using diffusion MRI and in vivo 1H MR spectroscopy. J Magn Reson Imaging, 41: 169-74.
95. Sah RG, Sharma U, Parshad R and Jagannathan NR (2009). Quantification of absolute concentration of choline for differentiation of malignant, benign and normal breast tissues by in-vivo proton MR spectroscopy. *Proc Intl Soc Magn Reson Med*, Hawaii, Honolulu, USA, 17.
96. Sah RG, Sharma U, Parshad R and Jagannathan NR (2010). Choline as a biomarker a better predictor of early response of breast cancer than tumor volume? Sequential study of the therapeutic response of locally advanced breast cancer patients undergoing neo-adjuvant chemotherapy (NACT). *Proc Intl Soc Magn Reson Med*, Stockholm Sweden, Europe, 18.
97. Sah RG, Sharma U, Parshad R, and Jagannathan NR (2012a). Cut-off values of the absolute concentration of total choline for the differentiation of early breast cancer, locally advanced breast cancer, benign and normal breast tissues using proton *in vivo* MRS in large cohort of women. *Proceedings of the 20th Annual Meeting of ISMRM*, Melbourne, Australia, P. 3001.
98. Sah RG, Sharma U, Parshad R, Seenu V, Mathur SR, Jagannathan NR (2012b). Association of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 status with total choline concentration and tumor volume in breast cancer patients: an MRI and in vivo proton MRS study. Magn Reson Med., 68: 1039-47.
99. Samani A, Zubovits J, Plewes DB (2007). Elastic moduli of normal and pathological human breast tissues: an inversion-technique-based investigation of 169 samples. Phys Med Biol., 52: 1565–1576.
100. Sardanelli F, Fausto A, Podo F (2008). MR spectroscopy of the breast. *Radiol Med.*, 113: 56-64. (Review).
101. Sardanelli F, Giuseppetti GM, Panizza P (2004). Italian trial for breast MR in multifocal/multicentric Cancer. Sensitivity of MRI versus mammography for detecting foci of multifocal, multicentric breast cancer in fatty and dense breasts using the whole-breast pathologic examination as a gold standard. *AJR of Roentgenol.*, 183: 1149-57.
102. Saslow D, Boetes C, Burke W, Harms S, Leach MO, Lehman CD, Morris E, Pisano E, Schnall M, Sener S, Smith RA, Warner E, Yaffe M, Andrews KS, Russell CA (2007). American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *Cancer J. Clin*., 57: 75-89.
103. Schnall, M.D., Blume, J., DeAngelis, G.A. et al. (2006). Diagnostic architectural and dynamic features at breast MR imaging: multicenter study. Radiology, 238: 42–53.
104. Sharma U, Agarwal K, Sah RG, Parshad R, Seenu V, Mathur S, Gupta SD, Jagannathan NR (2018). Can Multi-Parametric MR Based Approach Improve the Predictive Value of Pathological and Clinical Therapeutic Response in Breast Cancer Patients? Front Oncol., 15; 8: 319.
105. Sharma U, Baek HM, Su MY, Jagannathan NR (2011). *In vivo* ^{1}H MRS in the assessment of the therapeutic response of breast cancer patients. Article first published online: DOI: 10.1002/nbm.1654.
106. Sharma U, Danishad KA, Seenu V, Jagannathan NR (2009). Longitudinal study of the assessment of tumor response of locally advanced breast cancer patients undergoing neoadjuvant chemotherapy by MR imaging and diffusion weighted imaging. *NMR Biomed.*, 22: 104-13.
107. Sharma U, Jagannathan NR (2010). Breast magnetic resonance spectroscopy (MRS), In: Encyclopedia of Magnetic Resonance, Eds. RK Harris and RE Wasylishen, John Wiley: Chichester. DOI: 10.1002/9780470034590 emrstm1167.
108. Sharma U, Sah G.R, Jagannathan NR (2008). Magnetic Resonance Imaging (MRI) and

Spectroscopy (MRS) in Breast Cancer. *Magnetic Resonance Insights*, 2: 93-108.
109. Sharma U, Sah RG, Agarwal K, Parshad R, Seenu V, Mathur SR, Hari S, Jagannathan NR (2016). Potential of Diffusion-Weighted Imaging in the Characterization of Malignant, Benign, and Healthy Breast Tissues and Molecular Subtypes of Breast Cancer. Front Oncol., 23; 6: 126.
110. Sharma U, Sah RG, Parshad R, Sharma R, Seenu V, Jagannathan NR. Role of apparent diffusion coefficient values for the differentiation of viable and necrotic areas of breast cancer and its potential utility to guide voxel positioning for MRS in the absence of dynamic contrast-enhanced MRI data. Magn Reson Imaging, 2012; 30: 649-55.
111. Shin HJ, Baek HM, Ahn JH, Baek S, Kim H, Cha JH, Kim HH (2012). Prediction of pathologic response to neoadjuvant chemotherapy in patients with breast cancer using diffusion-weighted imaging and MRS. *NMR Biomed.;* doi: 10.1002/nbm.2807. (Epub).
112. Shin HJ, Kim HH, Ahn JH, Kim SB, Jung KH, Gong G, Son BH, Ahn SH (2011). Comparision of mammography, sonography, MRI and clinical examination in patients with locally advanced or inflammatory breast cancer who underwent neoadjuvant chemotherapy. *Br J Radiol.*, 84: 612-20.
113. Siegmann KC, Krämer B, Claussen C (2011). Current Status and New Developments in Breast MRI. *Breast Care (Basel)*, 6: 87-92. (Review).
114. Sijens PE, Wijrdeman HK, Moerland MA, Bakker CJ, Vermeulen JW, Luyten PR (1988). Human breast cancer *in vivo*: ^{1}H and 31P MR spectroscopy at 1.5T. *Radiology*, 169: 615-20.
115. Sinkus, R., Siegmann, K., Xydeas, T. et al. (2007). MR elastography of breast lesions: understanding the solid/liquid duality can improve the specifi city of contrast-enhanced MR mammography. Magn. Reson. Med., 58: 1135-44.
116. Sonmez G, Cuce F, Mutlu H, Incedayi M, Ozturk E, Sildiroglu O, Velioglu M, Bashekim CC, Kizilkaya E (2011). Value of diffusion-weighted MRI in the differentiation of benign and malign breast lesions. *Wien Klin Wochenschr.*, 123: 655-61.
117. Stanwell P, Gluch L, Clark D, Tomanek B, Baker L, Giuffrè B, Lean C, Malycha P, Mountford C (2005). Specificity of choline metabolites for *in vivo* diagnosis of breast cancer using ^{1}H MRS at 1.5 T. *Eur Radiol.*, 15: 1037-43.
118. Stanwell P, Mountford C (2007). *in vivo* proton MR spectroscopy of the breast. *Radiographics*, 27: S253-66. (Review).
119. Stomper PC, Winston JS, Herman S, Klippenstein DL, Arredondo MA, Blumenson LE (1997). Angiogenesis and dynamic MR imaging gadolinium enhancement of malignant and benign breast lesions. *Breast Cancer Res. Treat*., 45: 39-46.
120. Tabár L, Vitak B, Chen TH et al (2011) Swedish two-county trial: impact of mammographic screening on breast cancer mortality during 3 decades. Radiology, 260: 658–663.
121. Tan PC, Lowry M, Manton DJ, Turnbull LW (2006). Evaluation of choline concentrations in malignant breast lesions in predicting response to neoadjuvant chemotherapy. *Proc Intl Soc Magn Reson Med*,; Seattle, Washington, USA, 14.
122. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012 (2015). CACancer J Clin., 65(2): 87–108.
123. Tozaki M, Hoshi K (2010a). 1H MR spectroscopy of invasive ductal carcinoma: correlations with FDG PET and histologic prognostic factors. AJR Am J Roentgenol., 194: 1384-90.
124. Tozaki M, Oyama Y, Fukuma E (2010b). Preliminary study of early response to neoadjuvant chemotherapy after the first cycle in breast cancer: comparison of 1H magnetic resonance spectroscopy with diffusion magnetic resonance imaging. Jpn J Radiol., 28: 101-9.
125. Tozaki M, Sakamoto M, Oyama Y, O'uchi T, Kawano N, Suzuki T, Yamashiro N, Ozaki S, Sakamoto N, Higa K, Abe S, Ogawa T, Fukuma E (2008). Monitoring of early response to neoadjuvant chemotherapy in breast cancer with 1H MR spectroscopy: comparison to sequential 2-[18F]-fluorodeoxyglucose positron emission tomography. J Magn Reson Imaging, 28: 420-7.
126. Tse GM, Tan PH (2010). Diagnosing breast lesions by fine needle aspiration cytology or core biopsy: which is better? *Breast Cancer Res Treat.*, 123: 1-8.
127. Türkbey B, Aras Ö, Karabulut N, Turgut AT, Akpinar E, Alibek S, Pang Y, Ertürk ŞM, El Khouli RH, Bluemke DA, Choyke PL (2012). Diffusion-weighted MRI for detecting and monitoring cancer: a review of current applications in body imaging. *Diagn Interv Radiol.*, 18: 46-59.
128. Von Goethem M, Tjalma W, Schelfout K, Verslegers I, Biltjes I, Parizel P (2006). Magnetic resonance imaging in breast cancer. *Eur J Surg Oncol.*, 32: 901-10.
129. Warner E, Messersmith H, Causer P, Eisen A, Shumak R, Plewes D (2008). Systematic review: using magnetic resonance imaging to screen women at high risk for breast cancer. *Ann Intern Med.*, 148: 671-9.
130. Warren RM, Thompson D, Pointon LJ, Hoff R, Gilbert FJ, Padhani AR, Easton DF, Lakhani SR, Leach MO (2006). Collaborators in the United Kingdom Medical Research Council Magnetic Resonance Imaging in Breast Screening (MARIBS) Study. *Radiology*, 239: 677-85.
131. Woodhams R, Kakita S, Hata H, Iwabuchi K, Umeoka S, Mountford CE, Hatabu H (2009). Diffusion-weighted imaging of mucinous carcinoma of the breast: evaluation of apparent diffusion coefficient and signal intensity in correlation with histologic findings. *AJR Am J Roentgenol.*, 193: 260-6.

132. Woodhams R, Matsunaga K, Iwabuchi K, Kan S, Hata H, Kuranami M, Watanabe M, Hayakawa K (2005a). Diffusion-weighted imaging of malignant breast tumors: the usefulness of apparent diffusion coefficient (ADC) value and ADC map for the detection of malignant breast tumors and evaluation of cancer extension. *J Comput Assist Tomog.,* 29: 644-9.
133. Woodhams R, Matsunaga K, Kan S, Hata H, Ozaki M, Iwabuchi K, Kuranami M, Watanabe M, Hayakawa K (2005b). ADC Mapping of Benign and Malignant Breast Tumors. *Magn Reson Med Sci.,* 4: 35-42.
134. Wu LM, Hu JN, Gu HY, Hua J, Chen J, Xu JR (2012). Can diffusion-weighted MR imaging and contrast-enhanced MR imaging precisely evaluate and predict pathological response to neoadjuvant chemotherapy in patients with breast cancer? *Breast Cancer Res Treat.;* (Epub).
135. Xydeas, T., Siegmann, K., Sinkus, R. et al. (2005). Magnetic resonance elastography of the breast: correlation of signal intensity data with viscoelastic properties. Invest. Radiol., 40: 412–20.
136. Yankeelov TE, Lepage M, Chakravarthy A, Broome EE, Niermann KJ, Kelley MC, Meszoely I, Mayer IA, Herman CR, McManus K, Price RR, Gore JC (2007). Integration of quantitative DCE-MRI and ADC mapping to monitor treatment response in human breast cancer: initial results. *Magn. Reson. Imaging,* 25: 1-13.
137. Yeung DK, Cheung HS, Tse GM (2001). Human breast lesions: Characterization with contrast-enhanced *in vivo* proton MR spectroscopy-initial results. *Radiology,* 220: 40-6.