



EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

Directorate F - Health, Consumers & Reference Materials (Ispra)
Health in Society

European Commission Initiative on Breast Cancer (ECIBC): European guidelines on breast cancer screening and diagnosis

QUESTION	
Should tailored screening with digital breast tomosynthesis (including synthesised 2D images) vs. digital mammography be used for early detection of breast cancer in asymptomatic women with high mammographic breast density in organised screening programmes?	
POPULATION:	asymptomatic women with high mammographic breast density.
INTERVENTION:	tailored screening with digital breast tomosynthesis (DBT) (including synthesised 2D images)
COMPARISON:	mammography alone
MAIN OUTCOMES:	Breast cancer mortality, breast cancer stage, interval breast cancer, breast cancer detection, recall for assessment, mastectomy, provision of chemotherapy, adverse effects (including radiation exposure, radiation-induced cancers-related to radiation dose, overdiagnosis related adverse effects, false-positive related adverse effects).
SETTING:	European Union
PERSPECTIVE:	Population (National Health System)
BACKGROUND:	<p>Breast cancer is the second most common cancer in the world and, by far, the most frequent cancer among women, with an estimated 2 088 849 new cancer cases diagnosed in 2018 (11.6% of all cancers), it ranks as the fourth cause of death from cancer overall (626 679 deaths) (1).</p> <p>Screening programmes play a crucial role in early breast cancer detection; they can increase the chance of survival as well as reduce disease specific mortality. Mammography remains the best method to detect breast cancer in an early stage. However, mammography has a lower sensitivity and specificity in women with radiologically dense breasts (2). The use of different screening strategies including other imaging modalities, in addition to mammography, might improve early detection of breast cancer in women with higher mammographic breast density.</p> <p>Digital breast tomosynthesis (DBT) is an imaging technique based on a series of low dose images of the breast taken from different angles and one compression, and has the potential to partly overcome tissue superposition thus improving detection of breast lesions through minimization of masking effects in DM ((3), (4)). The series of projections is then processed by a reconstruction algorithm to estimate the 3D appearance of the breast which can be viewed in successive slices. In screening trials, tomosynthesis has been used in addition to a 2D image done with 2D DM, regardless whether synthetic 2D images of the DBT series were available or not.</p> <p>Dense breast tissue is made up mostly of ductal structures and connective tissue, while non-dense breast tissue is mostly fatty. Breast density is seen only on mammograms.</p> <p>Due to lack of evidence using the breast density BIRADS (Breast Imaging Report and Database System) classification edition 5, the</p>

	<p>GDG decided to base the recommendation on the previous breast density BIRADS classification assuming that the results are comparable for the two versions. Therefore, for the purpose of this clinical guideline, one of the following criteria classifies as dense breast:</p> <p>(1) BIRADS category scale: III-IV score.</p> <p>(2) For studies reporting quantitative percent density, a dense area of 50% as roughly equivalent to BIRADS III-IV (BIRADS III would be 50-75% and BI-RADS IV would be greater than 75%).</p> <p>(3) For those studies reporting the old Wolfe categories: BIRADS III would be P2 and BIRADS IV corresponding DY.</p>
CONFLICT OF INTEREST:	<p><u>Management of Conflicts of Interest (Col)</u>: Cols for all Guidelines Development Group (GDG) members were assessed and managed by the European Commission Joint Research Centre (JRC) following an established procedure in line with the institutional rules. GDG member participation in the development of the recommendations was restricted, according to Col disclosure. Consequently, for this particular question, the following GDG member was recused from voting: Axel Gräwingholt. Miranda Langendam, as external expert, was also not allowed to vote, according to the ECIBC rules of procedure.</p> <p>For more information please visit https://healthcare-quality.jrc.ec.europa.eu/discover-ecibc/governance/ecibc-working-groups</p>

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	<p>Breast cancer ranks as the fifth cause of death from cancer overall (522 000 deaths in 2012) and while it is the most frequent cause of cancer death in women in less developed regions (324 000 deaths), it is now the second cause of cancer death in more developed regions (198 000 deaths) after lung cancer (5).</p> <p>Breast cancer screening with additional screening modalities might improve the early detection of breast cancer in women with mammographically dense breast tissue. Although digital mammography (DM) has become an accepted standard of care in screening and diagnosis of breast cancer, up to 30% of breast cancers are not detected by standard screening (6). This percentage is even higher in women with dense breasts and in women under 50 years of age (2). In women with dense breasts, risk of breast cancer is increased (7), and cancers may be masked and missed on mammography due to superposition of tissue; as a result, there might be an excess of late stage disease (stages II and III) (8).</p>	<p>The GDG prioritised this question for the ECIBC.</p>

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS																								
<ul style="list-style-type: none"> ○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know 	<p>Date of last search: January 2020</p> <table border="1" data-bbox="520 329 1392 1049"> <thead> <tr> <th rowspan="2">Outcomes</th> <th rowspan="2">No of participants (studies) Follow up</th> <th rowspan="2">Certainty of the evidence (GRADE)</th> <th rowspan="2">Relative effect (95% CI)</th> <th colspan="2">Anticipated absolute effects* (95% CI)</th> </tr> <tr> <th>Risk with mammography alone</th> <th>Risk difference with tailored screening with digital breast tomosynthesis (DBT) (including synthesised 2D images)</th> </tr> </thead> <tbody> <tr> <td rowspan="2">Breast cancer detection</td> <td rowspan="2">5184 (1 observational study)^{1,a}</td> <td rowspan="2">⊕⊕○○ LOW^{b,c}</td> <td rowspan="2">RR 1.80 (1.04 to 3.10)</td> <td colspan="2">Study population</td> </tr> <tr> <td>772 per 100.000</td> <td>617 more per 100.000 (31 more to 1620 more)</td> </tr> <tr> <td rowspan="2">Adverse effects (false positive)</td> <td rowspan="2">5110 (1 observational study)^{1,a}</td> <td rowspan="2">⊕⊕○○ LOW^{c,d}</td> <td rowspan="2">RR 1.53 (1.20 to 1.96)</td> <td colspan="2">Study population</td> </tr> <tr> <td>3953 per 100.000</td> <td>2095 more per 100.000 (791 more to 3795 more)</td> </tr> </tbody> </table> <p>1. Bernardi, D., Gentilini, M. A., De Nisi, M., Pellegrini, M., Fanto, C., Valentini, M., Sabatino, V., Luparia, A., Houssami, N.. Effect of implementing digital breast tomosynthesis (DBT) instead of mammography on population screening outcomes including interval cancer rates: Results of the Trento DBT pilot evaluation. <i>Breast</i>; 2019.</p> <p>a. Cohort studies provided partial diagnostic information from paired analysis. The risk of bias was assessed using an ad-hoc modified QUADAS-2 tool.</p> <p>b. The results show imprecise estimates going from relevant decrease to increase in the breast cancer detection rate.</p> <p>c. Concerns for risk of bias due to reference standard was not blinded to the index tests. Additionally, there was variability in the number of readings, readers' experience, and the number of readers (i.e. single or double) across studies.</p>	Outcomes	No of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		Risk with mammography alone	Risk difference with tailored screening with digital breast tomosynthesis (DBT) (including synthesised 2D images)	Breast cancer detection	5184 (1 observational study) ^{1,a}	⊕⊕○○ LOW ^{b,c}	RR 1.80 (1.04 to 3.10)	Study population		772 per 100.000	617 more per 100.000 (31 more to 1620 more)	Adverse effects (false positive)	5110 (1 observational study) ^{1,a}	⊕⊕○○ LOW ^{c,d}	RR 1.53 (1.20 to 1.96)	Study population		3953 per 100.000	2095 more per 100.000 (791 more to 3795 more)	<p>There are 617 more breast cancers detected per 100 000 women screened and the proportion of overdiagnosis in this population is less of a concern. The GDG agreed the desirable effects were moderate.</p> <p>One diagnostic study with random allocation of participants, reported data for recall rate, however, no data were reported for breast cancer detection, which precludes the interpretation of this estimate (9).</p>
Outcomes	No of participants (studies) Follow up					Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)																		
		Risk with mammography alone	Risk difference with tailored screening with digital breast tomosynthesis (DBT) (including synthesised 2D images)																							
Breast cancer detection	5184 (1 observational study) ^{1,a}	⊕⊕○○ LOW ^{b,c}	RR 1.80 (1.04 to 3.10)	Study population																						
				772 per 100.000	617 more per 100.000 (31 more to 1620 more)																					
Adverse effects (false positive)	5110 (1 observational study) ^{1,a}	⊕⊕○○ LOW ^{c,d}	RR 1.53 (1.20 to 1.96)	Study population																						
				3953 per 100.000	2095 more per 100.000 (791 more to 3795 more)																					

d. The results show imprecise estimates going from relevant decrease to increase on the false positive rate.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS																								
<ul style="list-style-type: none"> ○ Large ● Moderate ○ Small ○ Trivial ○ Varies ○ Don't know 	<p>Date of last search: January 2020</p> <table border="1" data-bbox="520 440 1415 1062"> <thead> <tr> <th rowspan="2">Outcomes</th> <th rowspan="2">No of participants (studies) Follow up</th> <th rowspan="2">Certainty of the evidence (GRADE)</th> <th rowspan="2">Relative effect (95% CI)</th> <th colspan="2">Anticipated absolute effects* (95% CI)</th> </tr> <tr> <th>Risk with mammography alone</th> <th>Risk difference with tailored screening with digital breast tomosynthesis (DBT) (including synthesised 2D images)</th> </tr> </thead> <tbody> <tr> <td rowspan="2">Breast cancer detection</td> <td rowspan="2">5184 (1 observational study)^{1,a}</td> <td rowspan="2">⊕⊕○○ LOW^{b,c}</td> <td rowspan="2">RR 1.80 (1.04 to 3.10)</td> <td colspan="2">Study population</td> </tr> <tr> <td>772 per 100.000</td> <td>617 more per 100.000 (31 more to 1620 more)</td> </tr> <tr> <td rowspan="2">Adverse effects (false positive)</td> <td rowspan="2">5110 (1 observational study)^{1,a}</td> <td rowspan="2">⊕⊕○○ LOW^{c,d}</td> <td rowspan="2">RR 1.53 (1.20 to 1.96)</td> <td colspan="2">Study population</td> </tr> <tr> <td>3953 per 100.000</td> <td>2095 more per 100.000 (791 more to 3795 more)</td> </tr> </tbody> </table> <p>1. Bernardi, D., Gentilini, M. A., De Nisi, M., Pellegrini, M., Fanto, C., Valentini, M., Sabatino, V., Luparia, A., Houssami, N.. Effect of implementing digital breast tomosynthesis (DBT) instead of mammography on population screening outcomes including interval cancer rates: Results of the Trento DBT pilot evaluation. Breast; 2019.</p> <p>a. Cohort studies provided partial diagnostic information from paired analysis. The risk of bias was assessed using an ad-hoc modified QUADAS-2 tool.</p> <p>b. The results show imprecise estimates going from relevant decrease to increase in the breast cancer detection rate.</p> <p>c. Concerns for risk of bias due to reference standard was not blinded to the index tests. Additionally, there was variability in the number of readings, readers' experience, and the number of readers (i.e. single or double)</p>	Outcomes	No of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		Risk with mammography alone	Risk difference with tailored screening with digital breast tomosynthesis (DBT) (including synthesised 2D images)	Breast cancer detection	5184 (1 observational study) ^{1,a}	⊕⊕○○ LOW ^{b,c}	RR 1.80 (1.04 to 3.10)	Study population		772 per 100.000	617 more per 100.000 (31 more to 1620 more)	Adverse effects (false positive)	5110 (1 observational study) ^{1,a}	⊕⊕○○ LOW ^{c,d}	RR 1.53 (1.20 to 1.96)	Study population		3953 per 100.000	2095 more per 100.000 (791 more to 3795 more)	<p>The GDG agrees the undesirable effects related to radiation are minimally more using DBT compared to mammography.</p> <p>Approximately 2095 more false positives per 100 000 women screened. DBT increases false positives compared to DM alone.</p> <p>As there was disagreement among GDG members regarding whether the undesirable effects were small or moderate, voting took place among the 18 members without CoI: 11 GDG members voted that the effects were moderate. Five GDG members voted that the effects were small. Two GDG members abstained.</p>
Outcomes	No of participants (studies) Follow up					Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)																		
		Risk with mammography alone	Risk difference with tailored screening with digital breast tomosynthesis (DBT) (including synthesised 2D images)																							
Breast cancer detection	5184 (1 observational study) ^{1,a}	⊕⊕○○ LOW ^{b,c}	RR 1.80 (1.04 to 3.10)	Study population																						
				772 per 100.000	617 more per 100.000 (31 more to 1620 more)																					
Adverse effects (false positive)	5110 (1 observational study) ^{1,a}	⊕⊕○○ LOW ^{c,d}	RR 1.53 (1.20 to 1.96)	Study population																						
				3953 per 100.000	2095 more per 100.000 (791 more to 3795 more)																					

	<p>across studies.</p> <p>d. The results show imprecise estimates going from relevant decrease to increase on the false positive rate.</p>	
--	--	--

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Very low ○ Low ○ Moderate ○ High ○ No included studies 		<p>The GDG members agreed the overall certainty is very low. The certainty was low for test accuracy but as there is uncertainty about the downstream consequences, the overall certainty is very low.</p>

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes 	<p>No specific studies focusing in DM+DBT were identified. The findings are all from mammography studies (JRC Technical Report PICO 10-11, contract FWC443094012015; available upon request). However, the findings are likely to be generalisable DBT, as both screening tests are associated with similar desirable and undesirable effects (e.g. false positive findings or overdiagnosis). A systematic review shows that participants in mammography screening programmes place a low value on the psychosocial and physical effects of false positive results and overdiagnosis (JRC Technical Report PICO 10-11, contract FWC443094012015). Women generally consider these undesirable effects acceptable (<i>low confidence</i>).</p> <p>Date of last search: April 2016</p>	<p>The GDG agrees there is important uncertainty or variability around how much people value the main outcomes.</p>

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Favors the comparison ○ Probably favors the comparison ● Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know 		<p>The GDG agrees the balance of effects does not favour either the intervention or the comparison.</p>

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Large costs <input checked="" type="radio"/> Moderate costs <input type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <input type="radio"/> Varies <input type="radio"/> Don't know 	<p>Date of last search: January 2020</p> <p>No relevant economic evaluations were identified.</p>	<p>This assumes that the presence of breast density is known. The selection of the population on which you would do this intervention has a cost. We are taking a population perspective, this means only about 40% of all women would undergo this intervention, but costs were still considered to be moderate by the GDG.</p>

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input checked="" type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input type="radio"/> No included studies 		<p>The GDG agreed the certainty of the evidence of resource requirements is very low.</p>

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> No included studies 	<p>Date of last search: January 2020</p> <p>No relevant economic evaluations were identified.</p>	<p>No studies were included.</p>

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Reduced <input type="radio"/> Probably reduced <input type="radio"/> Probably no impact <input type="radio"/> Probably increased <input type="radio"/> Increased <input checked="" type="radio"/> Varies <input type="radio"/> Don't know 		<p>The GDG felt that within programmes there may be policy decisions to restrict them if there are increased costs and the programme is unable to fund universal participation.</p>

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <input checked="" type="radio"/> Varies <input type="radio"/> Don't know 	<p>Date of last search: April 2016</p> <p>No specific studies focusing on tomosynthesis (including synthetic 2D images) were identified. The findings, all from mammography studies, however, are likely to be generalizable to tomosynthesis (including synthetic 2D images) in addition to digital mammography, as both screening tests are associated with similar desirable and undesirable effects (e.g. false-positive findings or overdiagnosis). However, a systematic review (JRC Technical Report PICO 16-17, contract FWC443094032016; available upon request) found the following barriers associated with breast cancer screening with mammography: (a) lack of knowledge and misperceptions regarding preventive medicine and breast health (high confidence in evidence), (b) poor communication skills of healthcare providers (high confidence in evidence), (c) poor accessibility to breast screening, especially among women with disabilities (high confidence in evidence), (d) fear and stress related to the procedure and the possibility of cancer diagnosis (high confidence in evidence), (e) pain and discomfort during the procedure (moderate confidence in evidence), (f) embarrassment and shyness during the procedure (moderate confidence in evidence), (g) lack of support and encouragement from family members, caregivers and social network (moderate confidence in evidence), (h) lack of information regarding the available resources (low confidence in evidence) and (i) low prioritisation of breast cancer screening (low confidence in evidence). Women and relevant stakeholders expressed similar opinions.</p>	<p><u>Participants</u></p> <p>There may be variability in the acceptability for women as some may be concerned if in different programmes some women receive DBT and others DM.</p>

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <input checked="" type="radio"/> Varies <input type="radio"/> Don't know		One of the main barriers and challenges is to identify women with high breast density and tailor the intervention for this population.

SUMMARY OF JUDGEMENTS

PROBLEM	JUDGEMENT						
	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			No known undesirable outcomes
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

	JUDGEMENT						
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ●	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
---	--	---	--	---

CONCLUSIONS

Recommendation

For asymptomatic women, with high mammographic breast density, in the context of an organised screening programme, the ECIBC's Guidelines Development Group (GDG) suggests screening with either digital breast tomosynthesis (including synthesised 2D images) or digital mammography (conditional recommendation, very low certainty of the evidence).

Justification

This recommendation was agreed upon by consensus within the GDG with no need for voting.

The recommendation was made taking into consideration also the updated recommendation for using both tests (DBT and digital mammography) vs. digital mammography alone. The GDG considered that the desirable effect of higher breast cancer detection with DBT, compared to mammography, was moderate. The GDG considered that the undesirable effects related to radiation when using DBT were only minimally more compared to digital mammography (but double when using both DBT and digital mammography).

Subgroup considerations

The only subgroup assessed in this recommendation was women with high mammographic breast density.

Implementation considerations

The GDG members felt that information and education for women about dense breasts is critical. This includes information about limitations or uncertainty about the effects of tomosynthesis. For women with dense breast tissue, it is important that the context of increased risk and lesser accuracy of 2D mammography be explained. The opinion of women on tomosynthesis depends on the quality and impartiality of the education provided to them regarding the evidence behind this modality for tailored screening, including the limitations of tomosynthesis. The GDG members considered that this regimen would involve establishing a baseline, based on breast density, after the first examination, and a cut-off point which determines which women should be offered DBT.

There is a need for improvement in data management and storage for screening organisations. Women will have to attend a breast screening centre that has DBT technology available.

Monitoring and evaluation

Feasibility and acceptability could be assessed in the monitoring of programmes. Quality control procedures and quality standards should be further developed. Standards should be developed in particular for the image quality of synthesized 2D images from the tomosynthesis technology.

Research priorities

There is a need for research examining the classification of mammographic breast density and standardization of the classification systems used for breast density, including technology for the automation of the determination of breast density. Research should also aim at establishing the appropriate density threshold for changing imaging techniques. Further research is needed to build the evidence on benefits and harms of DBT vs DM through comparison of direct outcomes, including impacts of interval cancer incidence, stage of breast cancer at detection, and mortality reduction. There is also a need for research evidence on repeated DBT examinations since the current evidence is mainly restricted to a single surveillance episode. Trials in this area are ongoing and their results will influence the revision of this recommendation in the future. Further research should also assess the cost-effectiveness implications of tailored DBT screening for high mammographic breast density. Additional research should also assess the comparison between DBT and DM plus ultrasound for dense breast screening. Research is needed to define the quality parameters that need to be fulfilled for DBT-based breast cancer screening programmes to be implemented.

REFERENCES SUMMARY

1. Ferlay, J. Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: <https://gco.iarc.fr/today>, accessed [03/12/2018].; 2018.
2. Gilbert FJ, Tucker L,Gillan MG,Willsher P,Cooke J,Duncan KA,Michell MJ,Dobson HM,Lim YY,Purushothaman H,Strudley C,Astley SM,Morrish O,Young KC,Duffy SW.. The TOMMY trial: a comparison of TOMosynthesis with digital MammographY in the UK NHS Breast Screening Programme--a multicentre retrospective reading study comparing the diagnostic performance of digital breast tomosynthesis and digital mammography with digital mammography alone.. Health Technol Assess; 2015.
3. Rafferty EA, Park JM,Philpotts LE,Poplack SP,Sumkin JH,Halpern EF,et al.. Assessing radiologist performance using combined digital mammography and breast tomosynthesis compared with digital mammography alone: Results of a multicenter, multireader trial. Radiology; 2013.
4. Gur D, Abrams GS,Chough DM,Ganott MA,Hakim CM,Perrin RL,et al.. Digital breast tomosynthesis: observer performance study.. AJR American Journal of Roentgenology; 2009.
5. Ferlay, J, Soerjomataram, I , Ervik, M, Dikshit, R , Eser, S , Mathers, C, Rebelo, M, Parkin, DM, Forman, D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide. 2013.
6. Gilbert, F. J., Tucker, L., Gillan, M. G., Willsher, P., Cooke, J., Duncan, K. A., Michell, M. J., Dobson, H. M., Lim, Y. Y., Suaris, T., Astley, S. M., Morrish, O., Young, K. C., Duffy, S. W.. Accuracy of Digital Breast Tomosynthesis for Depicting Breast Cancer Subgroups in a UK Retrospective Reading Study (TOMMY Trial). Radiology; Dec 2015.
7. McCormack VA, dos Santos Silva I. Breast Density and Parenchymal Patterns as Markers of Breast Cancer Risk: A Meta-analysis. Cancer Epidemiol Biomarkers Prev; 2006.
8. Gierach GL, Ichikawa L,Kerlikowske K,Brinton LA,Farhat GN,Vacek PM,et al. Relationship between mammographic density and breast cancer death in the Breast Cancer Surveillance Consortium. J Natl Cancer Inst; 2012.
9. Aase HS, Holen AS,Pederson K,Houssami N,Haldorsen I,Seboudegard S et al.. A randomized controlled trial of digital breast tomosynthesis versus digital mammography in population-based screening in Bergen: interim analysis of performance indicators from the To-Be trial. European Radiology ; 2019.