

# 1 What is breast density?

Breast density is determined by the radiologist interpreting the mammogram and is assigned into one of four possible categories<sup>1</sup> (see below). Breast density as shown on mammography depends on the extent of fibrous and glandular tissue in the breasts and has no correlation with findings on palpation.

## Mammographic Breast Density Classification

Density	% of Breast Composed of Fibroglandular Tissue	ACR Category	% of Population <sup>2</sup>
Fatty	<25%	A	10%
Scattered fibroglandular	25 – 50%	B	43%
Heterogeneously dense	51– 75%	C	39%
Dense or Extremely dense	>75%	D	8%

# 2 How does breast density alter the ability of mammography to detect breast cancer?

Mammography alone is only 62-69% sensitive for the detection of breast cancer in women with heterogeneously dense or extremely dense breasts compared to 82-88% sensitive in women with lower breast density.

## Decreasing Mammography Sensitivity with Increased Breast Density

Density	ACR Category	Sensitivity <sup>3</sup> (%)
Fatty	A	88%
Scattered fibroglandular	B	82%
Heterogeneously dense	C	69%
Dense or Extremely dense	D	62%



More than 3 out of 4 women diagnosed with breast cancer in Canada are 50 or older.

# 3 What is the result of the decreased sensitivity of mammography in women with dense breasts?

Dense breast parenchyma can obscure small cancers (known as the masking effect)<sup>4</sup>. The risk of a patient presenting clinically with an interval cancer (between screening mammograms) is up to 18-fold higher comparing women at density extremes<sup>5</sup>. In the only series with sufficiently long-term follow-up to address mortality from breast cancer, Chiu et al.<sup>6</sup> observed a 1.9-fold risk of breast cancer death (95%CI 1.26–2.91) among women with dense breasts after adjusting for other factors.

# 4 How is breast density related to a women’s risk of developing breast cancer?

Women with dense breasts have an increased risk of developing breast cancer that is independent to all other risks factors (such as their family history). The increased amount of epithelial and stromal elements present in dense breasts means a greater risk that a cancer may arise<sup>7</sup>. Women with heterogeneously dense breasts may be 1.2-1.5 times more likely to develop breast cancer where as women with extremely dense breasts may be 2.1-2.3 times more likely<sup>8-14</sup>. By comparison, having a 1<sup>st</sup> degree family member with breast cancer makes a woman 1.8 or 3.3 times more likely to develop breast cancer in her lifetime depending on whether the family member was post or pre menopausal (respectively) when diagnosed<sup>15</sup>.

## Breast Cancer Risk Factors<sup>4-12</sup>

Risk Factor	Category of Risk	Comparison Category	Relative Risk (RR)
Alcohol Intake	2 drinks per day	Nondrinker	1.2
BMI	80 <sup>th</sup> percentile (age 55 or greater)	20 <sup>th</sup> percentile	1.2
Current Age	≥65 years	< 65 years	5.8
Past History of Breast Cancer	Invasive breast cancer	No history of invasive breast cancer	6.8
Family History	1 <sup>st</sup> degree relative ≥50 years with postmenopausal breast cancer	No 1 <sup>st</sup> , 2 <sup>nd</sup> -degree relative with breast cancer	1.8
	1 <sup>st</sup> degree relative with premenopausal breast cancer	No 1 <sup>st</sup> , 2 <sup>nd</sup> -degree relative with breast cancer	3.3
Breast Density	2 <sup>nd</sup> degree relative with breast cancer	No 1 <sup>st</sup> , 2 <sup>nd</sup> -degree relative with breast cancer	1.5
	Heterogeneously dense (ACR Category C)	Average breast density	1.2 - 1.5
	Extremely dense (ACR Category D)	Average breast density	2.1 - 2.3

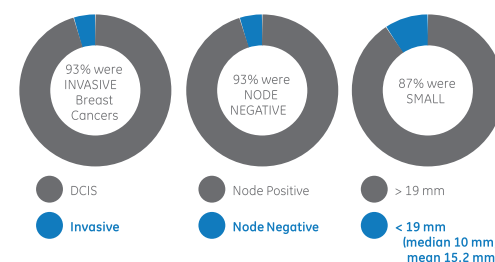
# 5 How does ABUS help cancer detection in women with dense breasts?

Increased breast density makes it easier to distinguish malignant lesions from the adjacent breast parenchyma. In average risk women with dense breasts, adding automated breast ultrasound (ABUS) to routine screening mammography increases the detection of breast cancer by 36-167%.

## Mammography Cancer Detection Rates (per 1,000) Alone and With ABUS

Density	N	Mammo alone	Mammo +ABUS	Rate Change	Rate Change (%)
Kelly <i>et al.</i> (2010) <sup>16</sup>	4,419	3.6	7.2	3.6	+100%
Giuliano <i>et al.</i> (2013) <sup>17</sup>	3,418	4.6	12.3	7.7	+167%
Brem <i>et al.</i> (2015) <sup>18</sup>	15,318	5.4	7.3	1.9	+36%
Wilczek <i>et al.</i> (2016) <sup>19</sup>	1,668	4.2	6.6	2.2	+52%
(Weighted Avg)	24,823	4.9	7.9	3.0	+66%

These cancers detected by ABUS tend to be small, invasive and node negative.



# 6 What are the risks of ABUS?

The two risks of ABUS for a patient are the increased risk of being recalled for supplemental imaging and an increased risk of ultimately undergoing a biopsy. The largest trial comparing mammography alone to mammography with supplementary ABUS (in average risk patients) showed that patients undergoing ABUS had an 89% increase of being recalled for additional imaging and a 93% increase rate of undergoing a breast biopsy<sup>18</sup>.

For patients coming to Toronto Centre for Medical Imaging, this could potentially increase our current mammography recall rate from 6% to 11%. Similarly, this could potentially increase the percentage of our screening patients ultimately undergoing biopsy from about 1% to 2%.

As a stand-alone test, ABUS had a lower false negative rate compared to mammography in women with dense breasts (15% vs. 27%, respectively)<sup>16</sup>. A very small but indeterminate number of cancers will be occult to both mammography and ABUS.

# 7 How should physicians incorporate ABUS into routine breast cancer screening?

All studies using ABUS to supplement screening mammography performed the tests concurrently at 1 year intervals<sup>16-19</sup>. Therefore for patients with dense breasts wishing to undergo screening mammography at one year intervals, yearly (concurrent) supplementary ABUS is most appropriate at present.

Patients with dense breasts that elect to undergo screening mammography every two years could undergo ABUS concurrent to mammography, alternating every year with mammography or have ABUS yearly.

# 8 What about using ABUS in women with non-dense breasts?

In average risk women with non-dense breasts, ABUS should not be used for supplemental imaging for two main reasons. Firstly, mammography has good sensitivity for breast cancer in women with low (ACR category A/B) breast density due to the lack of masking effect<sup>3</sup>. Secondly, there is poor ultrasound contrast between lesions and the adjacent tissues in women with non-dense breasts, hindering lesion detection.

# 9 What about using ABUS in screening programs for women at high risk for breast cancer?

Current guidelines recommend annual screening with both MRI and mammography for women considered high risk for breast cancer irrespective of breast density (eg. women with BRCA gene mutation). ABUS can be considered as another supplemental screening tool in certain clinical settings (eg. in women where MRI is contraindicated) but is an inferior substitute in high risk women as MRI has a higher cancer detection rate.



1 in 8 women will be diagnosed with breast cancer in their lifetime



75% of women who develop breast cancer have no family history.

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