

Additional Images for the article 'Breast Tissue Imaging Atlas using Ultra-Fast Confocal Microscopy to Identify Cancer Lesions' Marie-Christine Matthieu *et al.* **Virchows Archiv.**

## Master List and Legends

### Abbreviations

A: artefact

C: connective tissue

D: duct

DCIS : Ductal Carcinoma In Situ

F: fatty cells

I: inflammatory cells

IDC : Invasive Ductal Carcinoma

ILC : Invasive Lobular Carcinoma

IF: Indian Files

L: lobule

V: vessel

Normal Tissue	
1	<p><b>Normal Lobules 1</b></p> <p>Lobules (L) are composed of empty beads with purple circular wall. These beads are organized like a bunch of grapes. All the beads of a lobule are connected together with a branching structure of small pipes (small ducts). The present lobules are surrounded by normal connective tissue (C).</p>
2	<p><b>Normal Lobules 2</b></p> <p>The structures indicated by the green arrows are normal Lobules (L).</p>
3	<p><b>Normal Duct 1</b></p> <p>A large normal Duct is seen in the center (D). In this image, the walls of the duct are slightly folded and create some kind of funnel profile of the global structure. This allows the visualization of the duct's inner side composed of epithelial cells jointly evenly organized to form a cell layer. Cross section of the duct's cell wall can be seen and is normal because it is composed of thin layers of cells (*). This duct is surrounded by normal connective tissue (C), few fatty cells (F) and vessels (V).</p>
4	<p><b>Normal Duct 2</b></p> <p>A large normal duct is seen. Section of his thin normal wall is seen on the top part of the structure (1). This duct is unfolded to present the surface of the inner epithelial cells assembly on the bottom part of the structure (2). The lumen of the ducts is seen (*). This duct is surrounded by connective tissue.</p>
5	<p><b>Normal Duct 3</b></p> <p>A large normal duct is seen encircled in green. This duct is normal because it is not invaded by cancer cells: its lumen can be distinguished and its wall presents a thin appearance. This duct is surrounded by a large normal vessel (V) and connective tissue (C). A small normal lobule is seen at the bottom (L).</p>
6	<p><b>Normal Vessel</b></p> <p>This vessel (V) is surrounded by fatty tissue (F), connective tissue and lobules (L).</p>

7	<p><b>Connective tissue</b></p> <p>The green arrow is indicating normal Connective Tissue (C) that is more cellular. Cell-poor connective tissue can be seen in the other area of the image. Fatty cells (F) and vessels (V) are distributed in the connective tissue.</p> <p>A diagonal linear structure is an artefact (A) - probably a fiber coming from a compress or a paper towel.</p>
8	<p><b>Normal Tissue</b></p> <p>Normal connective and fatty tissues are seen in the image with small branched vessels.</p>
9	<p><b>Normal Tissue</b></p> <p>The green arrow is indicating a Vessel (V). The vessels are seen with the linear organization of cell wall nuclei.</p> <p>In this image, several vessels are seen in the matrix of fatty tissue (F).</p>
10	<p><b>Normal Tissue</b></p> <p>Vessels are seen surrounded by connective tissue with few fatty cells.</p>
11	<p><b>Normal Tissue</b></p> <p>A large normal vessel is seen within fatty tissue. This vessel is probably an artery with its thick wall composed of a low density of elongated cells (muscular cells).</p>
12	<p><b>Normal breast tissue</b></p> <ul style="list-style-type: none"> <li>- A normal lobule (L) is seen with its well defined circular structures organized like a bunch of grapes.</li> <li>- Different vascular structures are seen (V). As seen at the bottom, large vessels present in addition a striated pattern perpendicular to vessel direction (muscular cells of the vessel wall).</li> <li>- A large duct (D) is also seen. This duct is folded with its lumen seen as a inner white thin vertical line. In the present tissue section, this duct is mainly presenting its inner surface composed of epithelial cells seen. Epithelial cells are usually more purple than background tissue and are forming a jointly surface of large cell nuclei organized in a mosaic-like pattern. This pattern is quite similar to the pattern observed in the inner structures of the lobule seen on the left.</li> </ul>
13	<p><b>Muscular Fibers</b></p> <p>The present image is exclusively composed of normal muscular fibers. These fibers are seen here as large purple tubular structures. They are mainly organized in parallel form each other and with few cell nuclei localized on their borders.</p>

<b>Inflammatory changes</b>	
14	<b>Fatty tissue with inflammatory cells.</b> Aggregate of inflammatory cells (I) is seen at the bottom. Fatty tissue (F) and Vessels (V) can also be seen.
15	<b>Inflammatory tissue</b> A large structure of inflammatory cells is seen within the green annotation. Fatty (F*) and Connective (C*) tissues both infiltrated by inflammatory cells are also seen.
16	<b>Benign fibro-inflammatory tissue</b> It is mainly composed of inflammatory cells (small round and bright dots) and fibrous tissue (elongated nuclei lined up in the same direction). This tissue is surrounded by fatty cells.
17	<b>Inflammation</b> Benign tissue with elongated cells (fibroblasts) and few inflammatory cells can be seen. This pattern is typical of tissue reaction at the site of the biopsy taking.
18	<b>Fibro-inflammatory changes</b> It is mainly composed of inflammatory cells (small round and bright dots) and fibrous tissue (elongated nuclei lined up in the same direction). This type of tissue pattern is commonly seen at the site of the preoperative biopsy.
19	<b>Fibro-inflammatory tissue</b> Normal fatty tissue infiltrated with inflammatory cells is seen on the image. Inflammatory cells can be differentiated from invasive lobular carcinoma because they are smaller and present sharper borders.
20	<b>Inflammation</b> Two inflammatory infiltrates (I) are seen with their typical assembly of inflammatory cells recognized with their small and intense round nuclei very close from each other. They are invading fatty tissue (F). In the middle, there is a connective tissue (C) composed of fibroblasts with elongated nuclei. This type of architecture mixing inflammation and fibroblast-rich connective tissue is often found as the location of the preoperative biopsy sampling.
21	<b>Inflammation</b> The structure indicated by the green annotation is an inflammatory area (I). It is composed of typical inflammatory cells which present a high density of small and intense nuclei very close from each other. Connective tissue (C) and fatty tissue (F) are seen close to the inflammatory area. The area on the left without tissue architecture is an artefact composed of fluids with floating cells (A).

<b>Ductal Carcinoma In Situ</b>	
22	Two DCIS structures are seen. They are roundish patterns delimited by well-defined borders usually with bright coloration. These patterns are ducts filled with cancerous cells that present larger nuclei than normal cells. In the present case, cancerous cell nuclei are visualized with lighter coloration and slightly blurry. A cross-section of the DCIS is seen for the lesion on the right while a longitudinal section is seen for the larger DCIS on the left. These DCIS are surrounded by connective tissue (C) and by inflammatory cells (I) seen as bright and tiny purple dots.
23	Large roundish ducts containing cancer cells are seen in the image. As seen on the image, their lumen can be partly or completely filled by cancer cells with a micropapillary architecture.
24	Four DCIS structures are seen (encircled by red dotted lines). These roundish patterns are malignant ducts presenting well-defined borders and filled with cancerous cells. Here, cancer cells are filling completely the lumen of the ducts and are organized in a uniform pattern of jointed cells evenly distributed. DCIS are surrounded by fatty tissue with inflammatory cells (F*) and aggregates of inflammatory cells (I).
25	One large DCIS lesion is seen. Here the invaded duct can be figured out as a convoluted duct filled with cancer cells. Some inflammatory cells can also be seen in the DCIS as tiny dots strongly colored. This DCIS is surrounded by fatty tissue (F) that also contains few inflammatory cells.
26	A large roundish duct containing cancer cells is seen at the top of the image, its is not completely filled by cancer cells but the wall of the structure is very thick and composed of large cells tightly joined. A second DCIS structure is seen at the bottom. The rest is composed of connective tissue with inflammatory cells.
27	Large roundish ducts containing cancer cells are seen in the image. Their lumen are almost completely filled by cancer cells.
28	Many DCIS lesions can be seen encircled in red. They are found close to normal lobules (L). An artefact (fiber from paper towel or compress) is seen at the bottom (A).
29	One DCIS structure can be seen. In the DCIS, small empty spaces are typical of a cribriform architecture. This DCIS is surrounded by inflammatory cells (I).
30	Three sections of large DCIS structures are seen encircled in red. As usually, they are delimited by well-defined borders of bright coloration. The green annotation contains a high concentration of inflammatory cells (I) with their small nuclei of intense color.

	Roundish patterns can also be composed of inflammatory cells (#). They can be distinguished from DCIS by the sharpness, color intensity and size of the cell nuclei. As an illustration, a small DCIS structure (*) can be seen within inflammatory cells.
31	Three sections of large DCIS structures are seen encircled in red. As usually, they are delimited by well-defined borders of bright coloration. These ducts are filled with cancerous cells with large nuclei that are visualized with lighter coloration and slightly blurry. The green annotation is containing a high concentration of inflammatory cells (I) with their small nuclei of intense color organized around acini of a lobule (L/I).
32	A large duct completely filled with cancer cells is seen in the image. It is surrounded by a ring of inflammatory cells (I).
33	A large roundish duct filled with cancer cells is seen in the image. Its lumen is completely filled with cancer cells.

<b>Invasive Ductal Carcinoma</b>	
34	The right part of the image contains an IDC tumor core. It presents many features commonly seen for this cancer type: tumor nests (2), tubes (1) and a few indian files (IF). Inflammation (I) is seen in the periphery of the tumor core.
35	The present image is exclusively composed of an IDC tumor. This tumor is presenting many tumor nests and tubes haphazardly distributed (intense purple structures that are different in size and shape either circular or reminding duct-like structures). The connective tissue of this tumor core seen around these nests is also abnormal. It is hypercellular with strong remodeling seen as swirled patterns composed of elongated cell nuclei (fibroblasts). At the bottom left, tumor nests infiltrating fatty tissue can also be seen.
36	The image is showing a dense core of IDC infiltrating into fatty tissue.
37	This tumor is mainly composed of tumor nests haphazardly distributed. They are purple structures different in size and shape (either circular or reminiscent duct-like structures but with less defined borders) that are separated with white and cell-poor background. A single infiltrating tumor nest is seen within normal connective tissue within the red circle. A normal lobule is within the infiltrating nests (L). Some inflammation is also seen below the IDC red annotation (I).
38	The present image is mainly composed of an IDC tumor. This tumor core is presenting is composed of indian files of tumor cells and small tumor nests. Both are growing in a disorganized and chaotic fashion.

39	The image is showing tumor nests of IDC infiltrating into fatty tissue.
40	This image is exclusively composed of Invasive Ductal Carcinoma. It contains cancer cells organized in indian files patterns (*) and tumor nests (+). A large area composed of densely packed malignant epithelial cells is seen within the dotted circle (#).
41	A small focus of IDC in fatty tissue.
42	This tumor is mainly composed of cancer cells organized in indian files patterns. Some inflammation can be seen close to the IDC border, it is composed of high density of small and bright round cell nuclei (I). Two large normal vessel can be seen (V).
43	<b>IDC with DCIS</b> The IDC core has a chaotic architecture tumor nests of cancer cells, inflammatory cells and tissue remodeling. A cross-section of a DCIS lesion is seen. A cribriform pattern and a thin lumen of the duct is still visualized.
44	The image is showing a core of IDC exclusively composed of tumor nests of cancer cells.
45	<b>IDC with DCIS</b> The IDC is composed of cancer nests. A cross-section of a DCIS lesion is seen. Cancer cells from tumor nests of IDC and DCIS have a similar appearance. These cancerous lesions are surrounded by fatty tissue (F) infiltrated by inflammatory cells in some areas (F*). An aggregate of inflammatory cells can also be seen at the bottom right (I).
46	The image is showing IDC infiltrating into connective tissue. Its pattern is presenting dense tumor nests and few indian files of cancer cells. Inflammatory cells are seen within and around the IDC core.

<b>Invasive Lobular Carcinoma</b>	
47	The all image is showing an ILC tumor core infiltrating into fatty tissue. The present ILC presents an unstructured pattern. There is a complete loss of breast tissue morphology with strong remodeling. There is a high density of single cancer cells either haphazardly distributed, either organized under indian files patterns.
48	The image is showing an ILC tumor core. The present ILC presents an unstructured pattern. There is a high density of single cancer cells either haphazardly distributed, either organized under indian files patterns. This ILC is infiltrating into connective tissue (C).
49	Invasive Lobular carcinoma is seen on the right with typical strings of cancer cells infiltrating normal connective tissue (C).
50	The image is showing an ILC tumor core at the top part. The present ILC presents a dense unstructured pattern with few fatty cells. An aggregate of immune cells is also see to the right (I).
51	The right half of the image is showing an ILC tumor core. The present ILC presents a dense unstructured pattern on the top part while its bottom part is infiltrating into fatty tissue (F). An area with artefacts (A) composed of liquids is also seen close to the right border of the image. Remaining ducts and lobules are seen within the invasive tumor.
52	The image is showing an infiltration of ILC into fatty tissue. It presents a dense pattern with tumor nests aggregated and with few inflammatory cells at the interface with fatty tissue.
53	The image is showing a diffuse assembly of ILC cancer cells. Several indian cells can be seen and the tissue pattern is disturbed and not normal.
54	The image is showing an infiltration of ILC into connective tissue. It presents a disturbed pattern with strings of Indian files of cancer cells with few inflammatory cells.
55	The image is showing an infiltration of ILC into fatty tissue. It presents a disturbed pattern with Indian files of cancer cells and small tumor nests with few inflammatory cells.
56	The image is showing an infiltration of ILC into fatty tissue. It presents a diffused pattern of cancer cells arranged in indian files. Here the cancer cells looks bigger and brighter.