


Acellular dermal matrix imaging features in breast reconstructive surgery: a pictorial review

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Abstract

Acellular dermal matrices (ADMs) are biological engineered tissues, which may provide an immunologically inert scaffold in breast reconstruction. Since the literature on imaging features of ADMs is limited, radiologists must be aware of the common imaging appearances of ADM, to differentiate normal conformation from residual or recurrent disease. Our purpose is to review the current role of ADMs in implant-based breast reconstruction, describing the normal imaging findings at ultrasound, mammography, and MRI also considering the possible changes over time. In this pictorial essay, we reviewed imaging features of ADMs described in the literature and we reported our experience in patients who underwent reconstructive surgery with human or animal ADM for newly diagnosed breast cancer.

Keywords: acellular dermal matrix; breast reconstruction; mastectomy, imaging.

Introduction

Acellular dermal matrix (ADM) is a human, bovine, or porcine-derived biotechnologically engineered tissue (Figure 1) deprived of cells and antigens, that can trigger an immunologic response. It preserves the structural extracellular matrix that supports endogenous angiogenesis and tissue regeneration, to promote post-operative physiological healing with minimal resorption.¹⁻² Therefore, optimal ADMs show specific collagen and extracellular matrix components and should be recognized as host tissue for the patient, to induce minimal immune response. After a variable time, they should be re-populated by host cells, revascularized, and incorporated into the patient tissue.³

Acellular dermal matrices were first adopted for burn injuries treatment, abdominal wall repair, tympanic membrane replacement, dural repair, and gingival grafting.³ ADMs use was then extended to breast surgery field, specifically in revisional aesthetic surgery first, including correction of implant rippling, then in symmastia and soft tissue deficits. ADMs were furthermore applied to reconstructive surgery too, both in direct-to-implant (single-stage) than in two-stage implant reconstruction, representing a unique tool to improve aesthetic outcomes by expanding and reshaping the implant pocket, while further reducing the invasiveness of surgical intervention.³

The most frequent technique of heterologous breast reconstruction with scaffold support is the dual-plane subpectoral

approach, with partial muscular coverage of the implant: this technique involves the creation of a subpectoral pocket followed by inferomedial elevation and precise division of the pectoralis major muscle from the inferior margin. The ADM is then sutured inferiorly to the inframammary fold and laterally to the chest wall along with the anterior axillary line. The device (either tissue expander or permanent implant) is then inserted beneath the pectoralis-ADM layer, and the ADM is sutured to the free margin of the pectoralis major muscle (Figure 2). The main disadvantages of submuscular reconstruction include increased post-operative pain, animation deformity (represented by implant displacement with pectoralis muscle contraction), and decreased aesthetic outcomes. Another possible approach is the pre-pectoral breast reconstruction with ADM, which consists of the placement of a prosthesis in the pre-pectoral subcutaneous space, using an ADM to provide support and stability to the device and soft tissue coverage (Figure 3).⁴

The major benefits of ADMs of heterologous breast reconstruction include increased initial breast contouring, decreased risk of capsular contracture, and consistent stability of the reconstructed breast. On the other hand, ADMs may increase the risk of infection, seroma, and necrotic complications (ie, necrosis in mastectomy flap due to the possible greater intraoperative expansion of tissue expander), which may ultimately lead to implant loss, comparable with patients treated without them.⁵

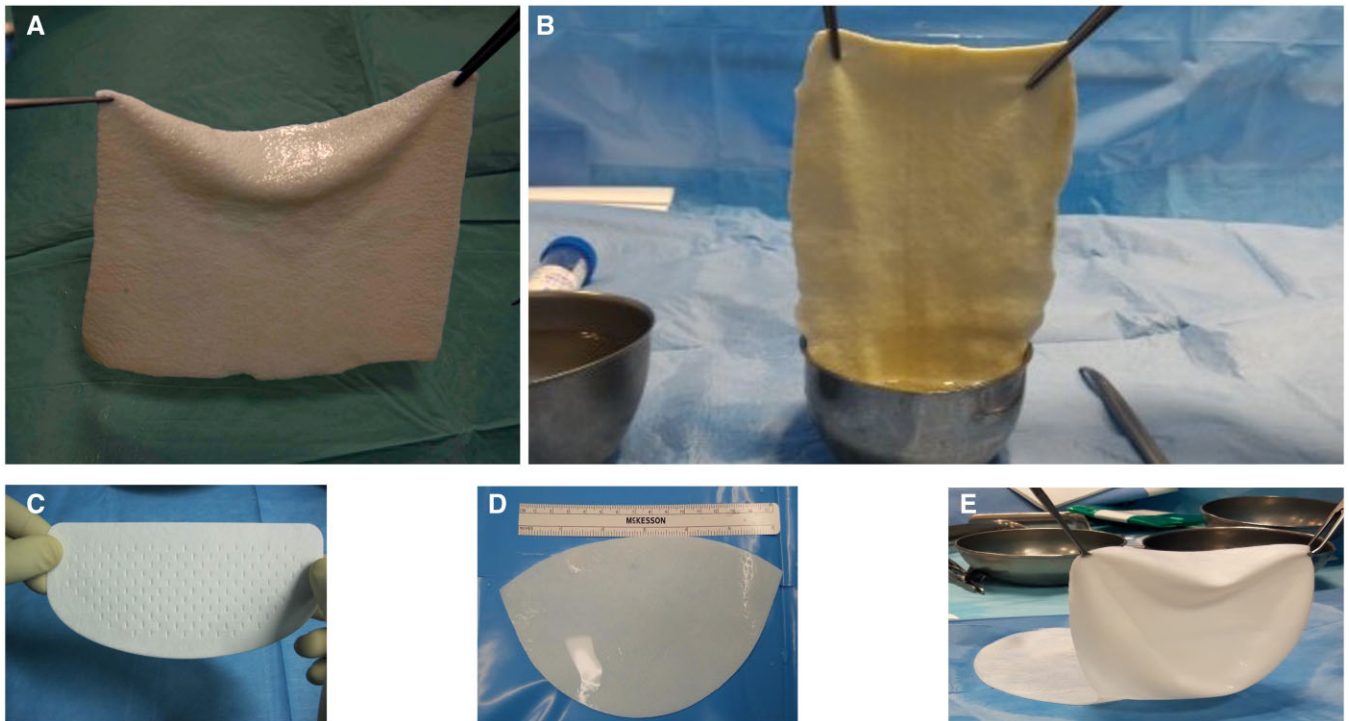


Figure 1. Acellular dermal matrix (ADM). Single sheets of human ADM from cadaver origin (A, B), ADM from bovine origin (C), ADM from porcine origin (D), and ADM from porcine origin conformed (E).

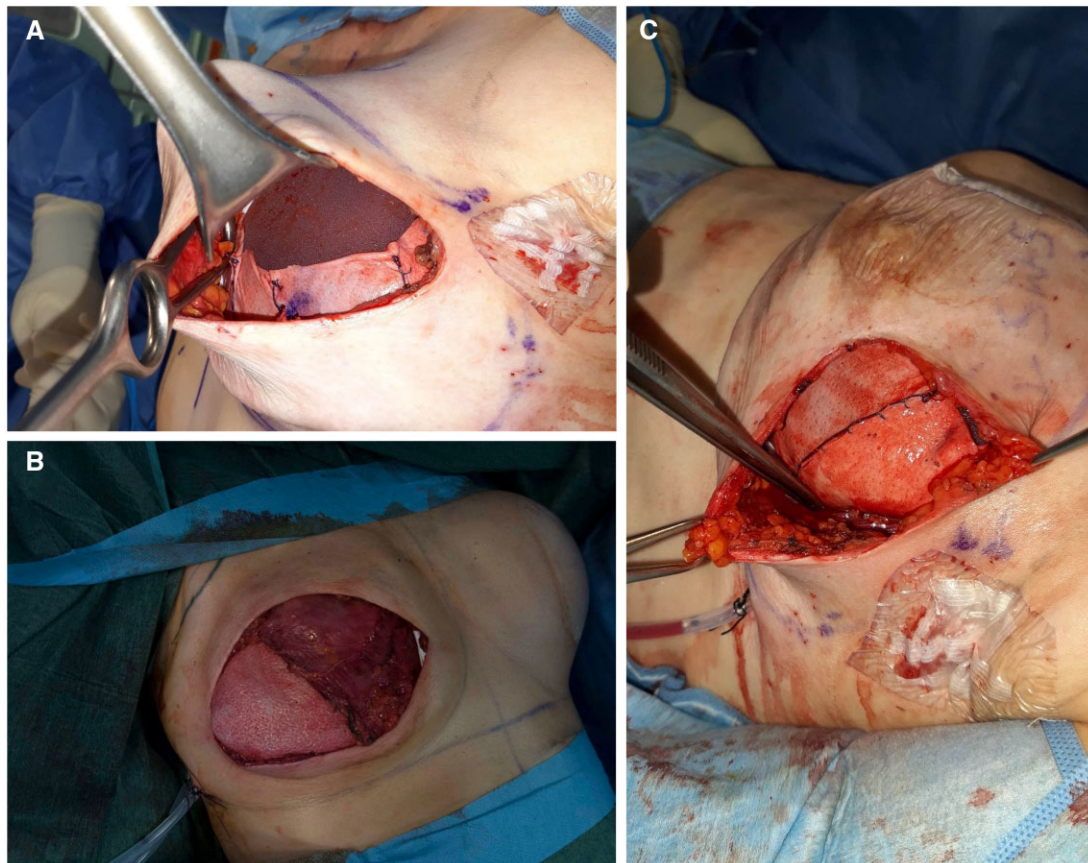


Figure 2. Implant-based breast reconstruction with human acellular dermal matrix (HADM). HADM from cadaver origin positioned to cover the inferior-lateral pole of the implant (A), then sutured to the free margin of the pectoralis major muscle to close the combined retro-muscular pocket (B), with complete HADM coverage of the implant underneath the skin incision (C).

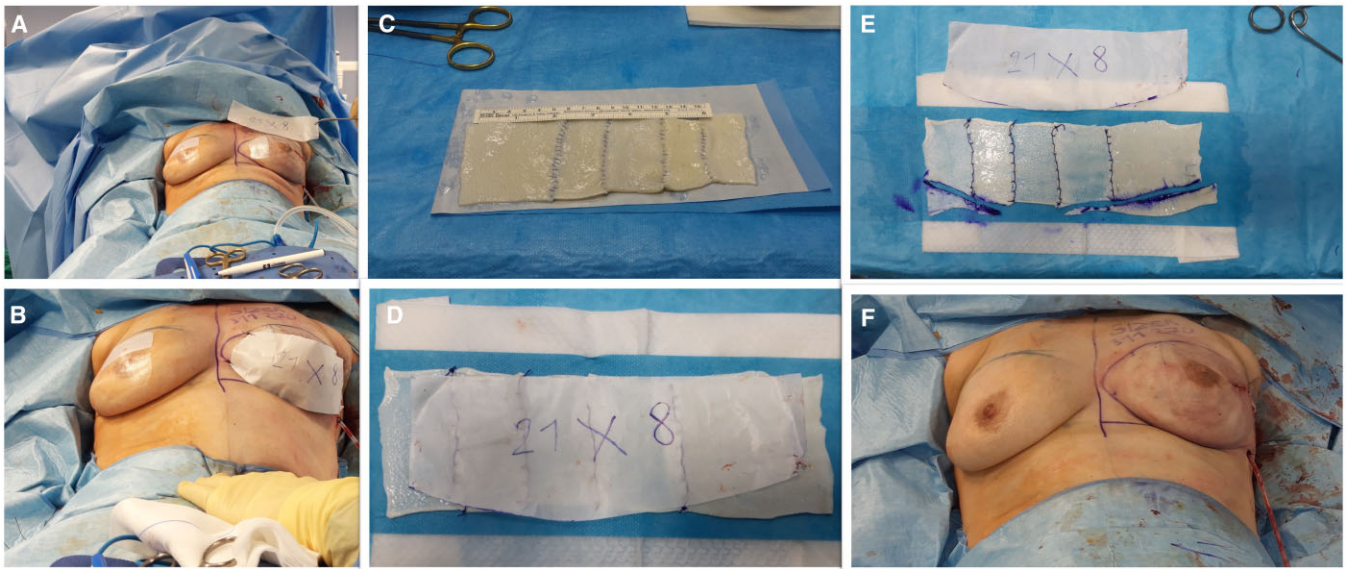


Figure 3. Pre-pectoral reconstruction with human acellular dermal matrix (HADM). (A, B) HADM's template shape and surface customized evaluation on the patient, for pre-pectoral reconstruction, (C) multiple HADM sheets sutured to the desired surface, (D) template positioned on the HADM, (E) HADM cut to the template, (F) surgical outcome after HADM and implant positioning.

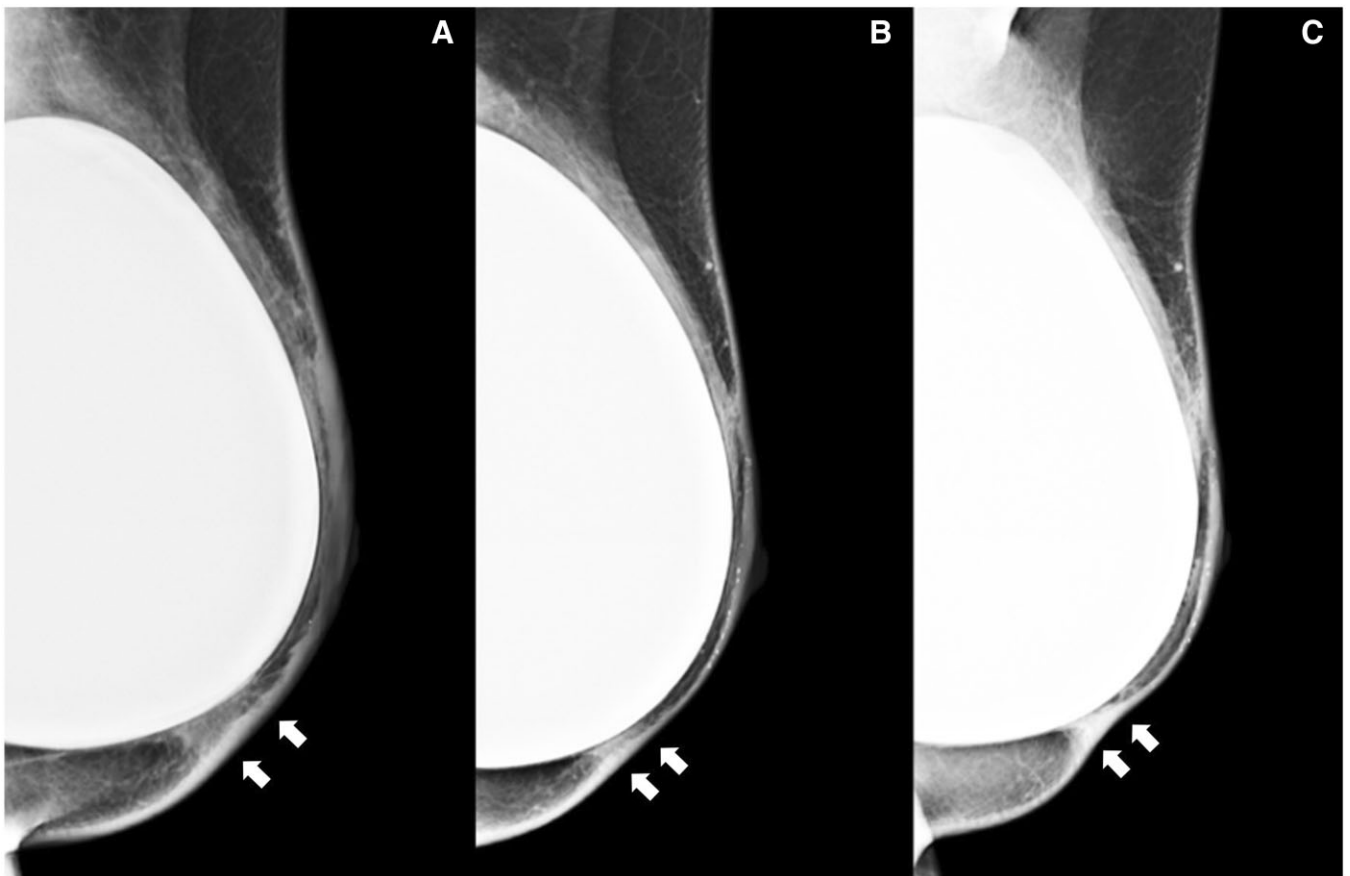


Figure 4. Animal acellular dermal matrix (ADM) mammographic features. Mammographic findings (medio-lateral oblique views) at 12 months after nipple-sparing mastectomy with implant-breast reconstruction using animal ADM: linear periprosthetic thickening (white arrows) in the lower quadrants associated with signs of oedema (A), reduced 12 months later (B), and with appearance of slight skin retraction 24 months later (C).

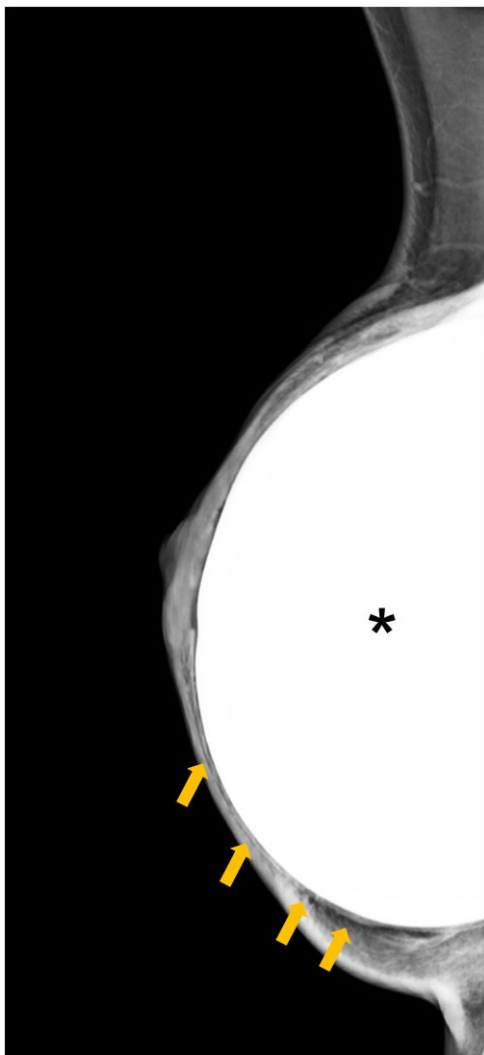


Figure 5. Human cellular dermal matrix (ADM) mammographic features. Mammographic findings (medio-lateral oblique view) at 12 months after nipple-sparing mastectomy with implant-breast reconstruction using human ADM: as for animal ADM, a linear periprosthetic thickening (yellow arrows) may be identified along the edge of the implant (black asterisk) in the lower quadrants; a diffuse skin thickening is also evident.

Acellular dermal matrices use can cause imaging misinterpretation during the follow-up period; the ADMs imaging features must be differentiated from postoperative local complications and ipsilateral tumour recurrence.⁶

Currently, literature reports very few studies or cases describing the imaging appearances of ADMs (both from animal and human origin) in breast reconstructive surgery patients. Therefore, the aim of this pictorial review is to describe the imaging features at mammography (MG), ultrasound (US), and MRI due to the presence of ADMs in breast reconstruction, also considering the possible imaging changes, over time.

ADMs mammographic features

In patients with breast reconstruction, MG can be performed in the two standard views (cranio-caudal and mediolateral oblique), also displacing the implant for the diagnostic evaluation of postoperative complications, palpable abnormalities, or pain. Mammographic images can show a prominent layer along the implant edge (Figures 4 and 5), or sometimes ADM appears as masses, isodense to the glandular tissue, not obscuring the conspicuity of calcifications.⁷ ADMs could resemble postoperative complications, such as seromas or haematomas too. Signs of oedema, consisting of overall increased parenchymal density, accentuated trabeculation, and increased skin thickness in the early preoperative phase, could be related to normal postoperative appearances but also be increased by the presence of ADM, decreasing over time.⁷

ADMs ultrasound features

At US, ADMs may appear as a hypoechoic periprosthetic layer, measuring less than a millimetre (0.3-0.6 mm) at 1 month after surgery till 1-3 mm in thickness afterwards⁸ (Figure 6). In the early (after 1 month) post-operative period, US examination may detect a membrane surrounded by a fluid film, separating the ADMs from both the prosthesis and the subcutaneous tissues with a progressive reduction of fluid collection during the follow-up.

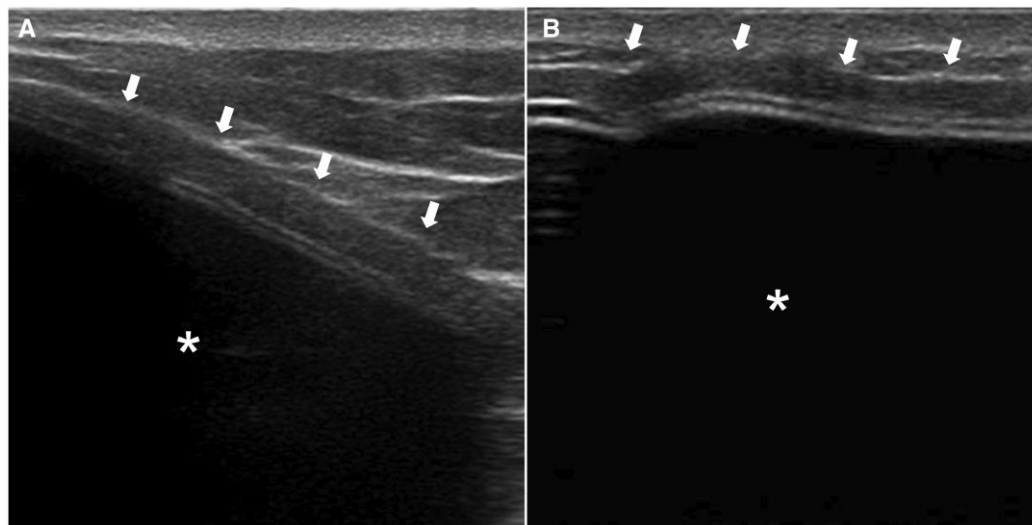


Figure 6. Acellular dermal matrix (ADM) ultrasound features. At ultrasound, ADM may be visible as a hypoechoic periprosthetic layer (white arrows) along the edge of the prosthesis (white asterisk) in the outer-lower (A) and inner (B) quadrants.

Moreover, the progressive host integration of the dermal matrix into the subcutaneous tissue, makes the tissue between the skin and the implant to increase its thickness.⁸⁻⁹

Another possible appearance is as a focal hypoechoic lesion contiguous to the implant profile (Figure 7) due to the merging of membrane folds: it was observed that the biological membrane was usually well stretched along the convexity of the implant's edge, while relaxed at the medial and lateral side of the implant where ADMs can curve and partially fold.⁸

In a recent study, Kim et al⁹ analysed the correlation between ADMs US features and their corresponding histopathological findings, performing ADM biopsy during second-stage surgeries (expander-implant exchanges) or implant replacements due to implant rupture or capsular contracture; preoperative skin marking was performed on the area showing abnormal US findings to directly compare histologic

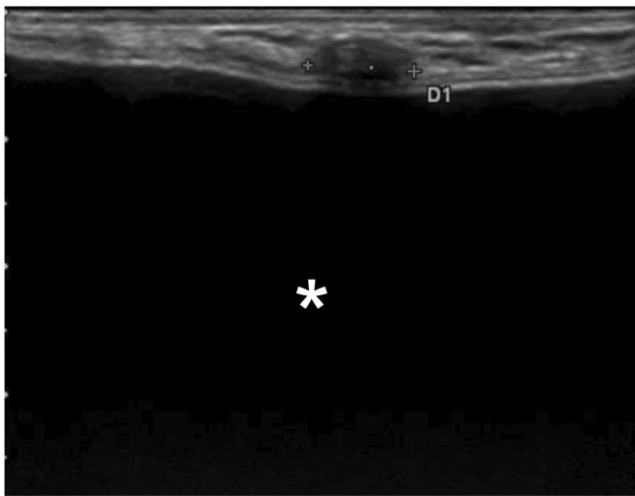


Figure 7. Acellular dermal matrix (ADM) at ultrasound. Breast ultrasound examination of 56-year-old woman who underwent skin sparing mastectomy: a focal hypoechoic lesion (palpable), contiguous with the implant profile (white asterisk), could be a concerning finding (recurrence versus surgical changes) if no other information is considered. As already reported in literature, patchy areas with chronic inflammatory infiltrate due to the ADM presence (as foreign-body) may represent a normal finding if an implant-breast reconstruction using ADM has been performed. In this case, the patient underwent skin sparing mastectomy using animal ADM: the US finding was unchanged during the follow-up.

findings. They highlighted how a focal thickening with decreased echogenicity may be due to a chronic inflammatory infiltrate, while a diffusely increased echogenicity may be related to dense collagen bundles. Another finding they described is bright echogenic spots inside of ADM layer, that histological analysis confirmed as empty spaces in which air was trapped during ADM creation.

These findings must be taken into consideration to correctly distinguish the normal evolution (Figure 8) of the matrix integration from other findings indicating disease recurrence (Figure 9).⁸

Ultrasound may easily differentiate ADMs from periprosthetic fluid collection, presenting as a thin and anechoic or corpuscolated layer along the edge of the implant. If considering fat necrosis as a differential diagnosis, US may evidence a hypoechoic nodule or mass with well-defined margins, evolving from inflammatory process into fat tissue: in such cases, clinical correlation helps to increase confidence in imaging diagnosis.⁷ Over time, ADMs cannot be identified by US anymore, because of their full integration into the host tissue, due to the high biocompatibility.⁸

Contrast-enhanced ultrasound is to be considered when evaluating vascular ingrowth of ADM, since initially showing encouraging results.¹⁰ Parvizi et al, in their case series, analysed over a period of 1-18 months postoperatively the morphological parameters as revascularization of ADMs and its integration into the surrounding tissue in relation to contrast enhancement. Homogeneous normal enhancement in the ADM and peripheral region with physiological tissue formation was seen in all patients.¹¹

ADM MRI features

On MRI images, in comparison with normal breast parenchyma, ADMs used for breast reconstruction are hyperintense on T2-weighted, isointense on T1-weighted imaging and show in early phase mild contrast enhancement, variable over time, looking like adjacent tissue after full incorporation into the host (Figures 10 and 11).⁷ ADMs could be seen overlying the implant or filling the gap between the skin and the implant. In their experience, Lee et al⁷ confirmed these data evaluating ADMs features in three separate cases of post-mastectomy reconstruction using different imaging modalities, including MRI. In the earlier study of Tran Cao et al,¹² who reported the use of ADM as a filler for lumpectomy

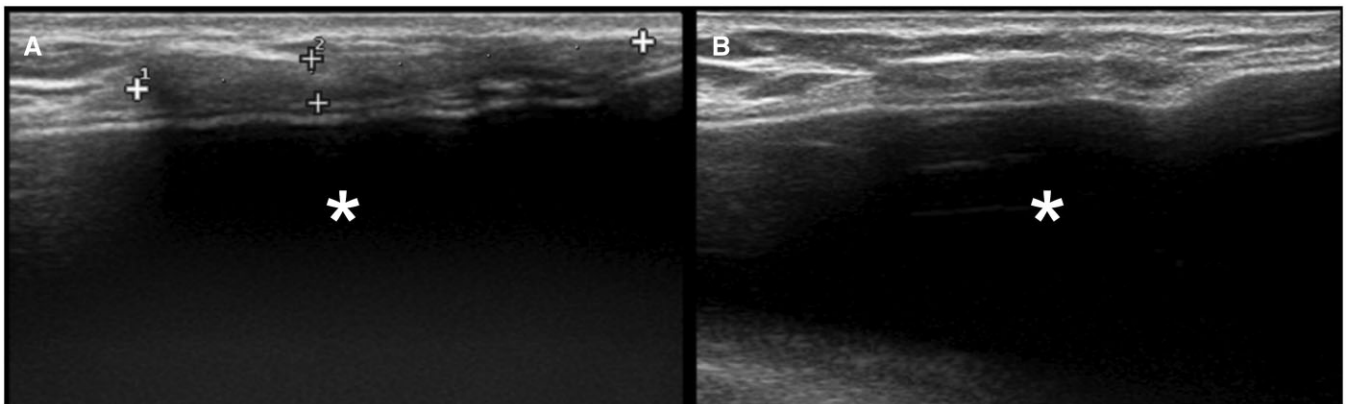


Figure 8. Acellular dermal matrix (ADM) at ultrasound: changes over time. Ultrasound view of animal ADM shows a homogeneous hypoechoic thickening along the edge of the prosthesis (white asterisk) at 12 months (A) after nipple-sparing mastectomy with implant reconstruction; 24 months later, the thinning of the periprosthetic layer (B) may suggest an initial integration.

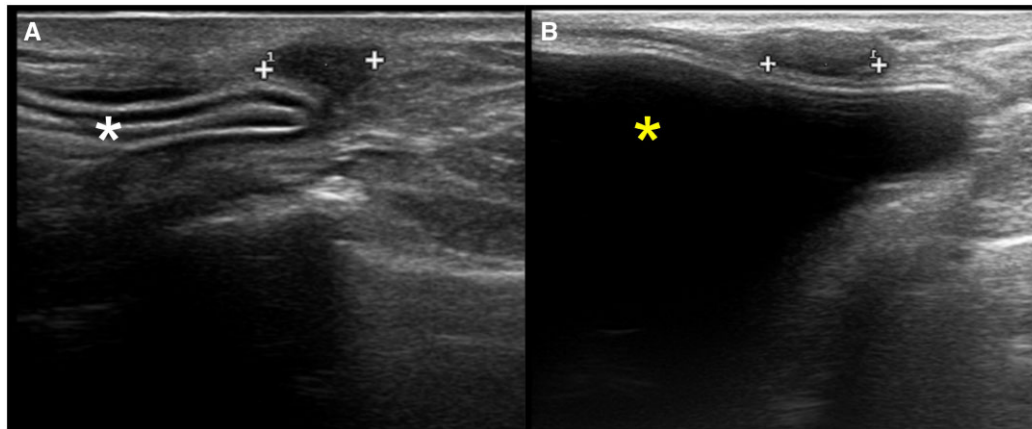


Figure 9. Acellular dermal matrix (ADM) at ultrasound: recurrence versus ADM findings. Breast ultrasound examination of a palpable lump in implant-breast reconstruction: (A) focal hypoechoic lesion, close to the skin expander profile (white asterisk), in skin sparing mastectomy without dermal matrix, resulting in a tumour recurrence after core-needle biopsy; (B) focal hypoechoic lesion, along the prosthesis profile (yellow asterisk), in skin-sparing mastectomy using animal ADM, representing a normal finding of dermal matrix, unchanged during the follow-up.

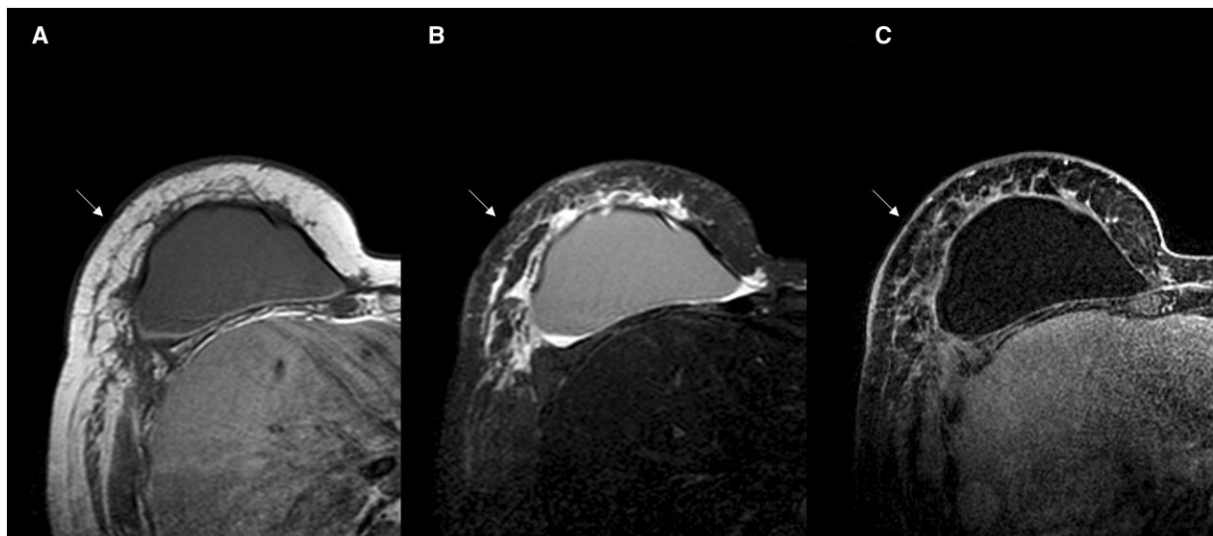


Figure 10. Human acellular dermal matrix (ADM) at MRI: normal findings. Twelve months after implant-breast reconstruction (skin-sparing mastectomy) with human ADM: breast MR imaging may show ADM as isointense periprosthetic layer on T1-weighted imaging (A), hyperintense on T2-weighted imaging (B), on post-contrast DCE sequences, ADM may demonstrate mild or no enhancement (C).

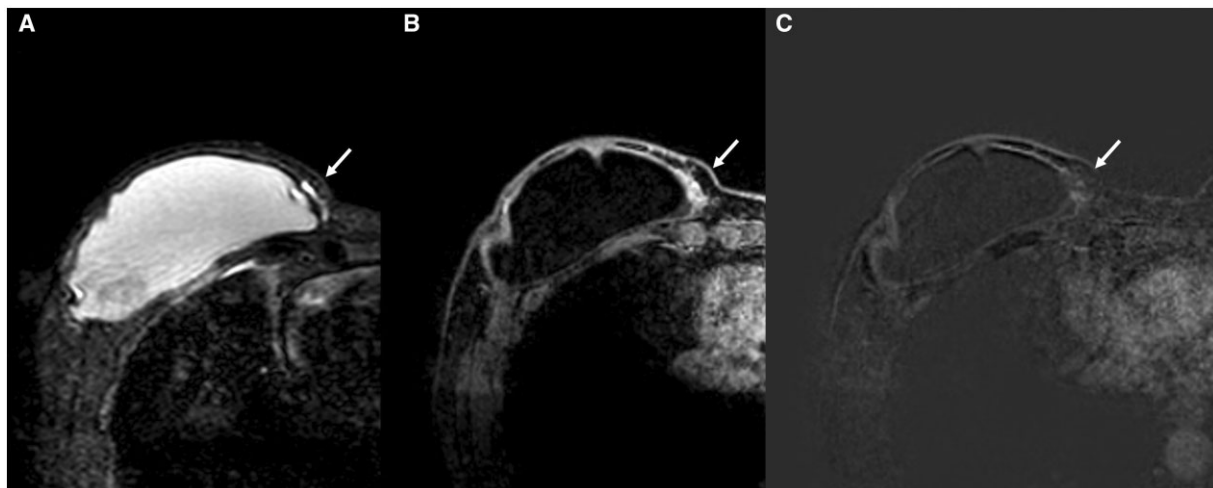


Figure 11. Animal acellular dermal matrix (ADM) at MRI: normal findings. Twelve months after implant-breast reconstruction (nipple-sparing mastectomy) with animal ADM: breast MR imaging show ADM along the inner edge of the implant as hyperintense on T2-weighted imaging (A) and on post-contrast DCE (B) and subtracted sequences (C) with mild contrast enhancement.

defects and a contouring device, ADM was described as hypointense to both glandular tissue and saturated fat on T2-weighted sequences, hypointense to fat and nearly isointense to glandular tissue on non-fat-saturated T1 sequences and showed no change in signal intensity after contrast administration (Figure 12). Despite the differences assessed in the unenhanced MRI sequences, both studies show that MRI enhancing features in the ADM location can be attributed to the elapsed time of incorporation into the host: MRI enhancement varies over time, with little if any enhancement

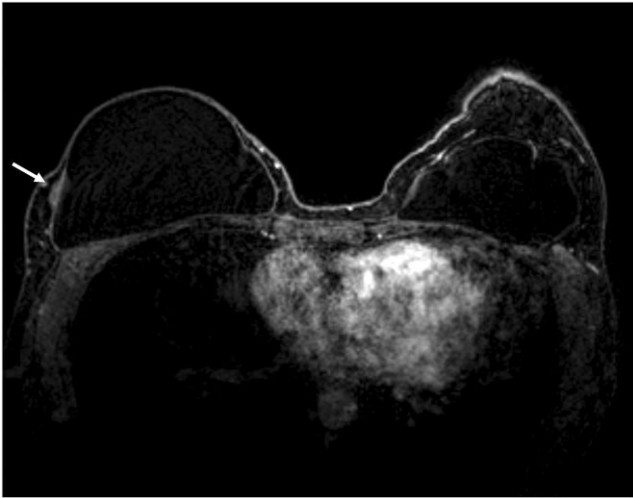


Figure 12. Acellular dermal matrix (ADM) at DCE-MRI. MRI view of focal pericapsular thickening without suspicious contrast enhancement in nipple-sparing mastectomy with human ADM implant-breast reconstruction.

of the matrix initially to similar enhancement to adjacent tissue after full incorporation into the host.⁷ Lee et al⁷ also reported that in one of the cases they evaluated, at the follow-up MRI after 16 months, less conspicuity and prominence of the non-mass enhancement in the ADM location were seen, assuming this would be related with interval incorporation of ADM into the host.

Tumour recurrence, that may occur within the reconstructed breast, can be distinguished from ADMs when occurring as a mass along the implant, with low signal intensity on T1-weighted images, low or intermediate signal intensity on T2-weighted images, and rapid, intense enhancement following administration of gadolinium (Figure 13). Other features, such as rim enhancement and spiculated morphology may lead to malignancy suspicion.¹ In the challenging cases, as for patients presenting with palpable mass, it is imperative that radiologists and surgeons could review the imaging together to determine where ADM was placed and elucidate if it correlates with the findings on imaging. MRI, that must be considered the most sensitive imaging for the detection of ipsilateral local tumour recurrence despite postoperative changes, can be a useful problem-solving tool in these cases, reassuring the decision making if no suspicious enhancement was found.

Clinical implication and conclusion

As the radiologic appearance of ADM is nonspecific and may depend on matrix reabsorption, distinguishing between ADM and disease recurrence on radiologic imaging is challenging.¹³ Radiologists must be aware that matrix reabsorption/biointegration is a dynamic process among inflammation (0-3 days), increased oxygen consumption and

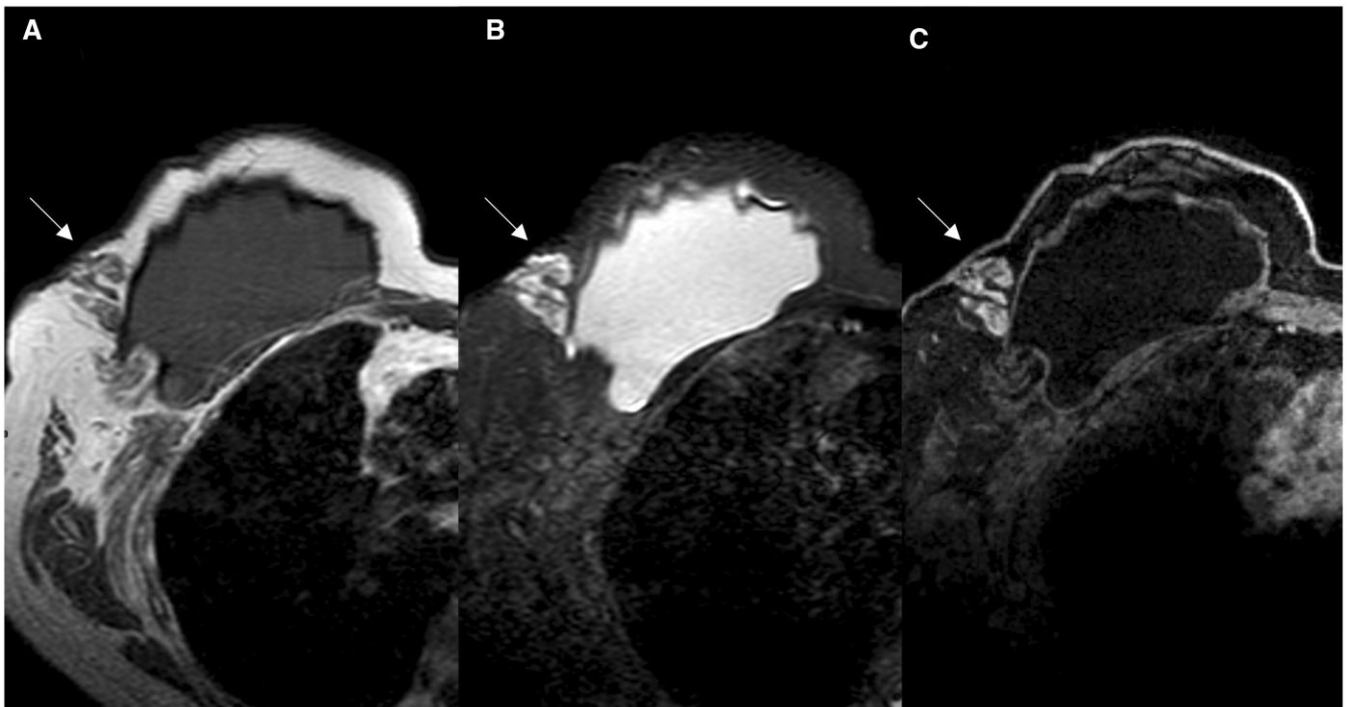


Figure 13. Local recurrence in breast implant reconstruction with acellular dermal matrix (ADM) at MRI. Sixty-four-year-old women who underwent nipple-sparing mastectomy using human ADM; MR images show the tumour recurrence in the upper-outer quadrant in the periprosthetic site, along the implant, resulting hypointense in T1-sequence (A), hyperintense in STIR (B), and with inhomogeneous contrast enhancement (C) on DCE-sequences.

neoangiogenesis at the matrix border (10-14 days), and vascular and inflammatory cell penetration into the centre of the matrix (>21 days),¹⁴ and thus ADMs appearance is variable during follow-up.

In the case of a palpable lump or clinical findings after breast reconstructive surgery following breast cancer, the diagnosis of a mass as ADMs rather than recurrence can be difficult. Such diagnostic imaging uncertainties result in short-term imaging and clinical follow-up, and sometimes, biopsy may be necessary for histopathological confirmation of a benign lesion.¹⁰

In equivocal cases of conventional diagnostic workup with MG and US, MRI can help to differentiate the conformation and configuration of ADMs from the remaining tissues of the reconstructed breast.⁷

The conformation of ADMs at surgical placement and its appearance during post-surgery must be taken into consideration when performing breast diagnostic imaging evaluation. The most helpful information should come from clinical history, correlation with the operative note (ie, type of reconstruction and timing), and direct discussion with the surgeon.

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Conflicts of interest

The authors declare to have no disclosures.

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