

October 6, 2017

**Important Update to Field Safety Notice**  
**Nellix® EndoVascular Aneurysm Sealing System**  
**Updated Instructions for Use (IFU)**

Dear Physician,

This notification is to provide you with further information on the Nellix EndoVascular Aneurysm Sealing System (Nellix System). Endologix is committed to using Field Safety Notices (FSNs) to share information that may impact patient outcomes. This communication takes the form of an update to the FSN issued in October 2016 for the Nellix System, and includes the current data available to support the refined IFU and patient selection criteria, options for secondary interventions in patients who have specific Nellix related complications, and information related to off-label use of the Nellix System. Please note this notice is for information only and no product return is required as a result of this notification. The Regulatory Agency of your country has been notified of this communication.

Endologix is committed to putting patients first in all we do. The Nellix System represents a novel endovascular aneurysm sealing (EVAS) therapy that is differentiated from conventional endovascular aneurysm repair (EVAR) modalities, and therefore we are continuing to monitor the clinical experience with the Nellix System, and provide updates on any important information that we learn.

***Refined IFU Assurance***

In the original FSN, Endologix updated the IFU with respect to the indications for use, patient selection criteria, and procedural best practices. The indications for use were revised to reduce the potential clinical risks of implant displacement (migration), Type I endoleaks, and/or aneurysm enlargement based upon the available 2-year clinical data from the first 58 US patients enrolled in the US investigational clinical trial (IDE Trial). Endologix has since gathered clinical data from 104 additional IDE Trial patients which have yielded consistent outcomes, thereby confirming that the criteria in the refined IFU reduced the risk of these clinical events. **Table 1** shows the comparison of the Freedom from rates for the On-label<sup>1</sup> and Off-label<sup>1</sup> IDE Trial patient population at 24 months relative to the refined indications for use introduced in October 2016.

**Table 1: Freedom from Event Estimates at 24 Months**

	<b>On-label Population</b>	<b>Off-label Population</b>
Freedom from Migration ≥10mm	97.7%	93.2 %
Freedom from Type Ia Endoleaks	99.0%	96.6%
Freedom from Aneurysm Enlargement >5mm	98.1%	93.5%

**Figure 1** below provides a graphical representation of the changes made to the indications for use with the corresponding anticipated clinical benefit.

As stated in the original FSN, there are currently two versions of the Nellix System commercially available, the Next Generation Nellix (i.e., Nellix 3.5) and Nellix 3SQ+, distinguishable via the product labeling. The

<sup>1</sup> On-label refers to the IDE Trial patient population that is within the indications for use in the refined IFU and Off-label refers to the IDE Trial patient population outside the indications for use in the refined IFU.

anticipated clinical benefits are consistent across both device versions. Based on differences however, related to the distal EndoBag to stent attachment between the Next Generation Nellix and Nellix 3SQ+, the revised indications for the distal iliac artery seal zone diameter for the Nellix 3SQ+ is slightly different as noted below.

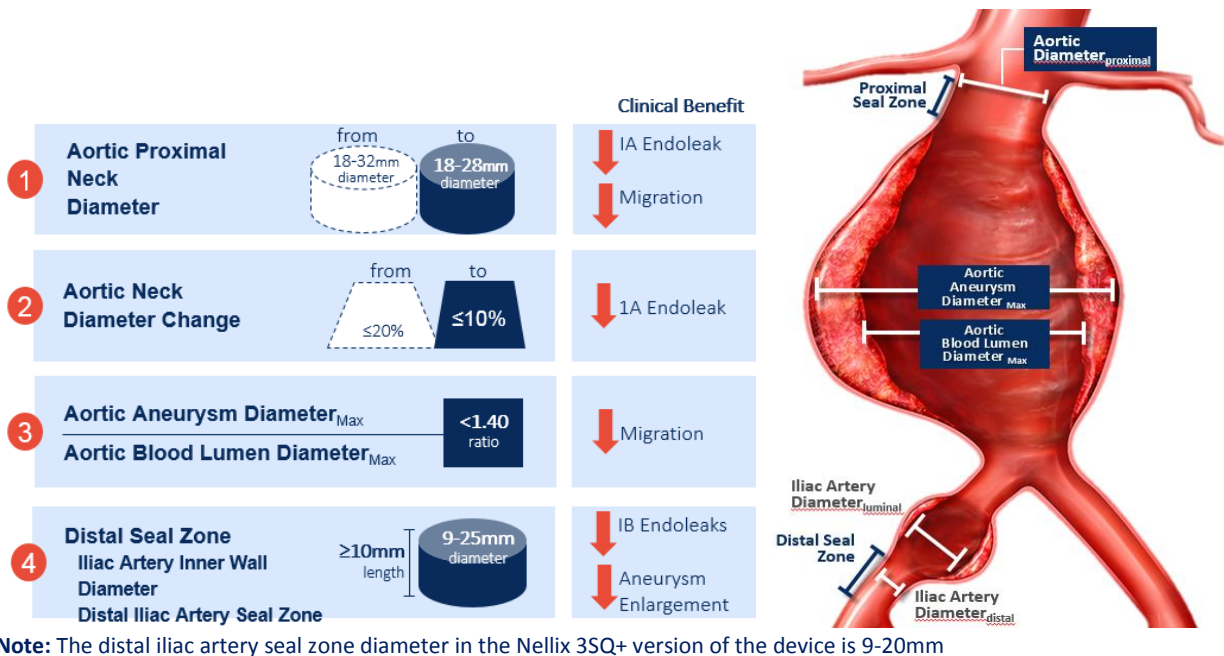


Figure 1: Refined Nellix Indications for Use with Corresponding Clinical Benefit

Note the revised indications for use were recently approved by Endologix’s Notified Body. Once translated, the complete, updated IFU will be provided either via hard copy upon request to Endologix Customer Service at +31 88 116 91 01 or made available in the Endologix Labeling Library, accessible as noted on the Nellix Catheter label (<http://www.e-labeling.eu/ELX10042> or ELX10041, depending on region) for countries where e-labeling is accepted.

### Recommended Patient Surveillance/Follow-up

The recommended follow up in the original FSN continues to apply: all patients require life-long, regular follow-up to assess the performance of their endovascular implant. Patients with specific clinical findings (i.e., changes in the structure or position of the endovascular implant, endoleaks, or enlarging aneurysms) should receive enhanced clinical and imaging follow-up. Specifically, patients should receive a contrast enhanced CT scan. If renal complications or other factors preclude the use of image contrast medium, abdominal radiographs and duplex ultrasound may provide similar information. **All asymptomatic patients should continue on annual follow-up, and this is particularly important for those who would now be considered off-label according to the refined IFU.** Additional secondary endovascular interventions (see below) or conversion to standard open surgical repair should be considered for patients continuing to experience migration, significant endoleaks, and/or enlarging aneurysms during post-operative follow up.

**Endologix does not recommend or endorse use of its products other than in accordance with their indications for use. The following information is being shared in the interest of patient safety only. Endologix has limited data for uses out of the scope of the intended use. Should a physician decide to use Nellix out of the intended use in the best interest of a patient, it is critical that the physician is sufficiently informed to evaluate this option.**

### ***Secondary Treatment Options for Patients with Significant Device Migration, Endoleaks, and/or Aneurysm Enlargement***

In consultation with physicians, Endologix has reviewed a range of secondary interventions from clinical studies, commercial use, literature, physician experience, and use in similar technologies (e.g., EVAR) to develop a list of recommended treatment options. Although all treatment options carry residual risks, the limited data support their consideration on a case-by-case basis. The treating physician should consider multiple factors such as subject anatomy, subject risk profile, hospital standard of care, and physician preference when determining what is best for each individual patient. Endologix's treatment recommendations described in **Attachment 1** are based on a subset of those factors, and as such, should be used as a reference for physicians and not a requirement. Endologix plans to disseminate specific details and conduct physician training (as needed) for each treatment option through the Office of Medical Affairs (OMA) upon physician request. The Office of Medical Affairs can be reached at [medicalaffairs@endologix.com](mailto:medicalaffairs@endologix.com).

### ***Off-Label Use of Nellix***

Endologix has become aware of the Nellix System being utilized off-label to treat complications stemming from failed EVAR and/or open repair procedures. The off-label use of the Nellix System in these situations often results in the use of small polymer fill volumes. In these cases, relatively small increases in polymer volume can result in a significant increase in pressure within the EndoBag. A rapid, sustained rise in EndoBag pressure can increase the risk of EndoBag prolapse and/or rupture. As such, should a physician decide that use of Nellix in this off-label manner is in the patient's best interests, it is critical that prefill and subsequent polymer is added carefully during the procedure, with adequate time for pressure readings to equilibrate between the EndoBag and the pressure transducer.

We will continue to monitor the clinical experience with the Nellix System, listen to physician feedback, and update you with any important information that we learn through our post-market surveillance programs. We appreciate your review of this notification and request that you share it within your organization as appropriate. If you have any questions regarding the content of this notification, please contact your Endologix representative or Endologix Customer service at +31 88 116 91 01.

Yours Sincerely,

A handwritten signature in blue ink, appearing to read "Matt Thompson".

Matt Thompson, MD  
Chief Medical Officer

## Attachment 1: Secondary Intervention Treatment Options (Note, clinical evidence to support the safety of these techniques is limited)

### Treatment Options for Isolated Migration

For isolated migration, when adequate proximal and distal seal is present and in the absence of endoleaks, one treatment option to consider is relining the entire length of each existing stent with an additional Nellix stent (no polymer), to provide resistance to lateral or anterior displacement. When adequate proximal and distal seal is present and the implant has migrated <10mm, Endologix recommends an option of routine surveillance utilizing either contrast or non-contrast computed tomography (CT). **Figure 2** provides an illustration of an isolated Nellix migration suitable for Nellix relining.

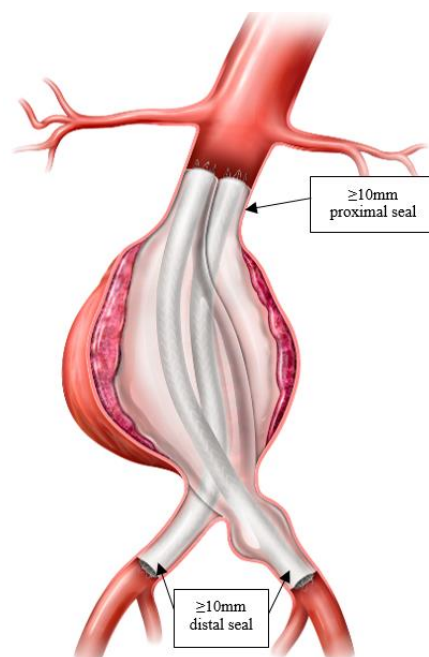
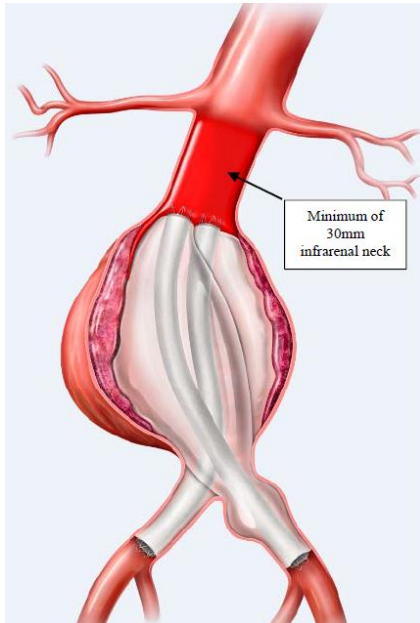


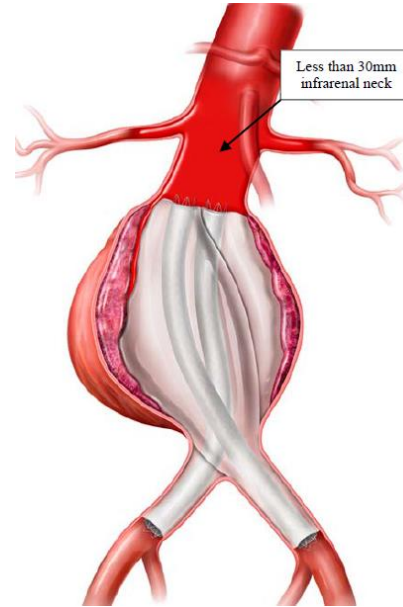
Figure 2: Example of Nellix Migration Suitable for Nellix Relining

### Treatment Options for Migration with Associated Type Ia Endoleaks

For subjects with migration and an associated Type Ia endoleak, options to consider include treatment with the Nellix device as a proximal extension, known as Proximal Extenders (when >30mm of infrarenal neck is available) and Proximal Extenders in conjunction with commercially available stent grafts in the visceral arteries (when <30mm of infrarenal neck is available). **Figure 3** provides an illustration of Nellix migration associated with Type Ia endoleak suitable for treatment with Nellix proximal extenders only while **Figure 4** provides an illustration of a Nellix migration associated with Type Ia endoleak, where both a Nellix proximal extender and visceral stent grafts are recommended.

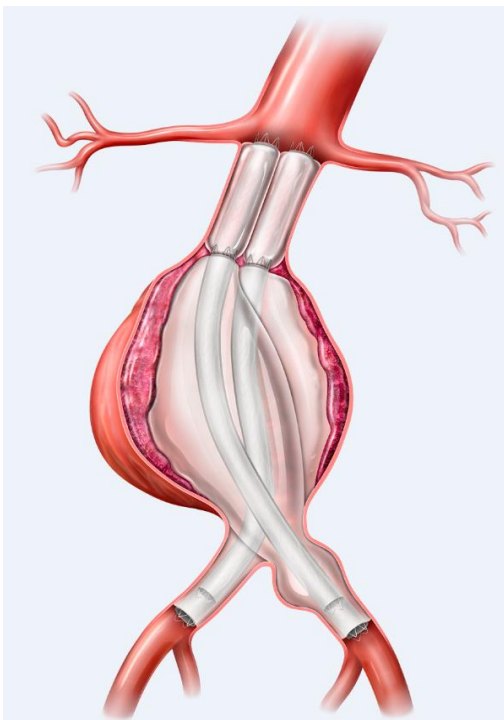


*Figure 3: Example of Migration and Type Ia Endoleak Suitable for Nellix Proximal Extenders*

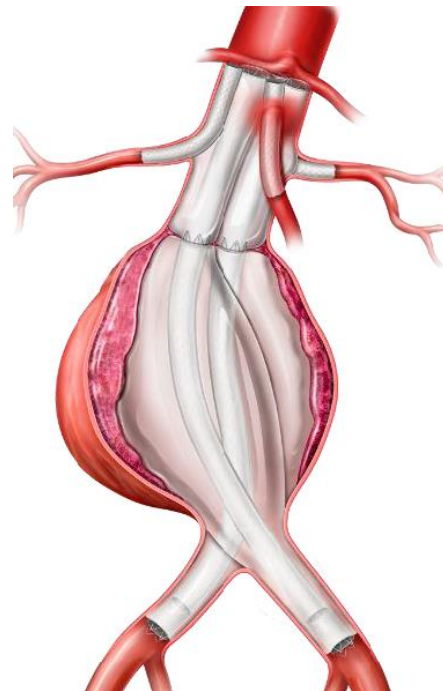


*Figure 4: Example of Migration and Type Ia Endoleak Suitable for Nellix Proximal Extenders with Commercially Available Stent Grafts in the Visceral Arteries*

**Figure 5** provides an illustration post-treatment with Nellix proximal extenders and **Figure 6** provides an illustration post-treatment with Nellix proximal extenders with commercially available stent grafts in the visceral arteries.



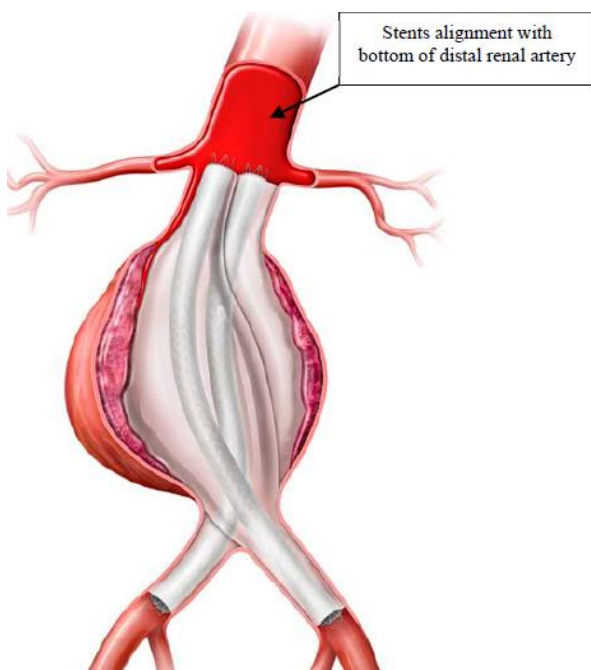
*Figure 5: Post-Treatment with Nellix Proximal Extenders*



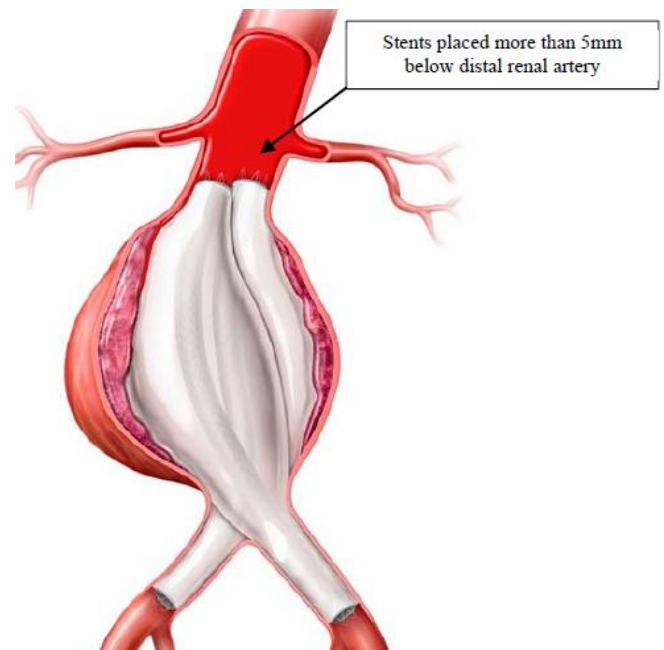
*Figure 6: Post-Treatment with Nellix Proximal Extenders and Commercially Available Stent Grafts in the Visceral Arteries*

### Treatment Options for Isolated Type Ia Endoleak

For subjects with isolated Type Ia endoleak (without migration), options to consider include treatment with coils/liquid embolics if the Nellix implant is positioned correctly (i.e. bottom of the first stent cell element is aligned with the distal origin of the most caudal renal artery) and coils/liquid embolics with commercially available proximal covered stents if the Nellix implant was positioned incorrectly (i.e. too far below the renal arteries), with a proximal seal of at least 10 mm. **Figure 7** provides an illustration of a Nellix Type Ia endoleak suitable for treatment with coils and liquid embolics only as the original Nellix stents are correctly positioned. **Figure 8** provides an illustration of a Nellix Type Ia endoleak suitable for coils and liquid embolics with proximal extension due to incorrect positioning of the original Nellix stents.

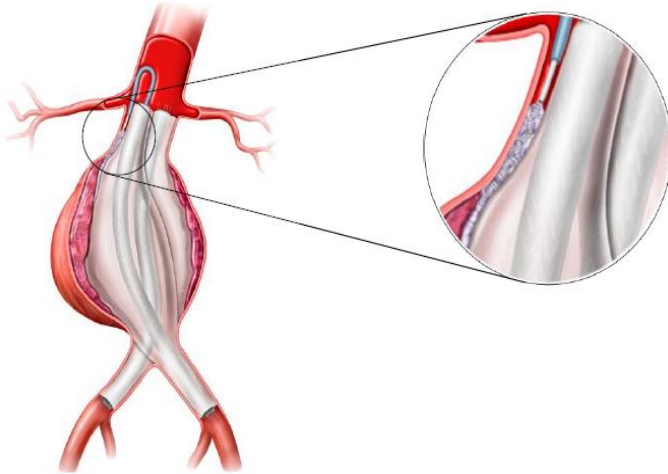


*Figure 7: Example of Nellix Type Ia Endoleak Suitable for Treatment with Coils and Liquid Embolics Only with Correct Stent Positioning*

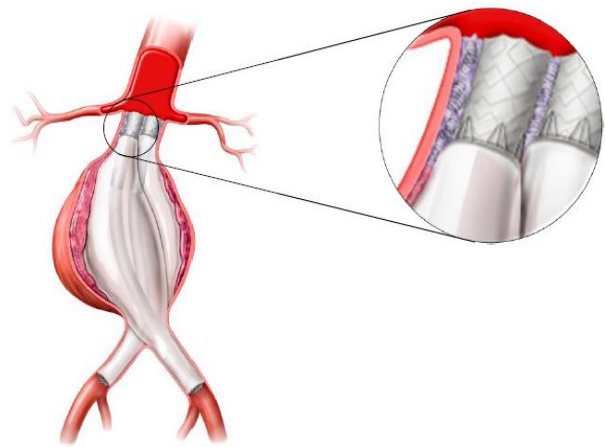


*Figure 8: Example of Nellix Type Ia Endoleak Suitable for Coils and Liquid Embolics with Proximal Extension Due To Incorrect Stent Positioning*

**Figure 9** provides an illustration post-treatment with coils and liquid embolics only and **Figure 10** provides an illustration post-treatment with coils, liquid embolics, and proximal extenders.



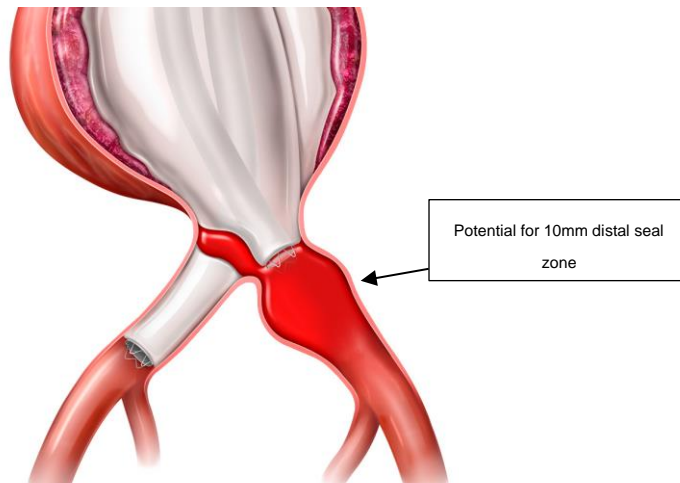
*Figure 9: Post-Treatment with Coils and Liquid Embolics Only*



*Figure 10: Post-Treatment with Coils, Liquid Embolics, and Proximal Extension*

#### **Treatment Options for Type Ib Endoleak**

For subjects with Type Ib endoleaks, a potential treatment option is use of the Ovation iX Iliac Stent Graft as a distal extender to re-establish the sealing zone. **Figure 11** provides an illustration of a Type Ib endoleak suitable for distal extension and **Figure 12** provides an illustration post-treatment with distal extenders.



*Figure 11: Example of Nellix Type Ib Endoleak Suitable for Distal Extension with the Ovation iX Iliac Stent Graft*

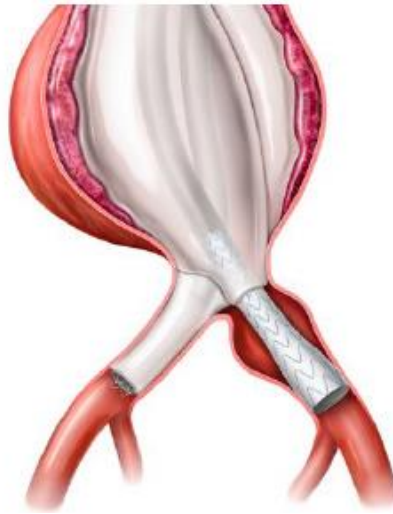


Figure 12: Post-Treatment with the Ovation iX Iliac Stent Graft Distal Extension

### Treatment Options for Aneurysm Enlargement

For subjects with aneurysm enlargement, if a Type Ia/Ib endoleak is present, treatment of the endoleak as described above may also address the aneurysm enlargement.

If aneurysm enlargement occurs in the absence of a Type Ia/Ib endoleak, one option to consider is treatment with an Ovation iX Iliac Stent Graft as a distal extender, as aneurysm enlargement may occur due to lack of apposition of the EndoBag to the arterial wall which allows pressurization of the aneurysm sac. As shown in **Figure 13** below, when there is an inadequate distal seal, the aneurysm sac can be pressurized due to the thrombus between the iliac artery and the distal portion of the Nellix implant. Pressurization of the aneurysm sac results in thrombus accumulation and aneurysm enlargement. To prevent further aneurysm enlargement, the distal seal between the iliac arterial wall and the EndoBag can be re-established with distal extension using the Ovation iX Iliac Stent Graft.



Figure 13: Image of Aneurysm Enlargement Caused by Pressurization