

Peer Review File

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Reviewer A

Comment 1: While the author poses an interesting question - what is the underlying etiology of capsular contracture, and can it be prevented - there is no data presented to make a definitive conclusion. This would benefit from data with capsular contracture rates when the pectoralis is denervated.

Reply 1: thanks indeed for your interest in my editorial. Actually, as for the part concerning selective muscular denervation yes, you are totally right there are no solid data in my paper to make a definitive conclusion, since being an editorial, and not an original study, I interpreted it as a “stone thrown into a pond” to raise some questions and observations about this topic. Although, the deduction implied in my hypothesis and in the ensuing proposal of denervation in case on retro-pectoral IBBR comes from many solid data and studies showing that pre-pec IBBR seems to clearly reduce the capsular contracture rate. Thus it is quite clear that avoiding the muscle use the rate of CC drops significantly. I reported more literature data and 4 more refs to clearly sustain this point, modifying also the paragraph about this topic to better explain my hypothesis. In case of retro-pec IBBR, apart from some encouraging results from ADM use or Polyurethane implants use, nothing has never been brought to be the solution. This novel approach, selective denervation, which I personally introduced few years ago, it is just at the beginning. An objective evaluation on CC is still missing and right now it is only a hint to move in the direction I believe might be the solution, namely preventing muscular contractions. In the first study on this novel technique, which I published (17), there is a series of 56 procedures with patient-reported subjective evaluation. I have another article in press with 50 more patients, but still with a subjective evaluation by means of Breast-Q (the Covid restrictions on F-UP in the last year at our Institution stopped me from an objective evaluation on the CC rate in this cohort, being a non necessary outpatient visit). Moreover, there is a very recent paper of a former colleague of mine, Casella D, who reported a series of 62 patients submitted to pectoralis major muscle denervation with very good results in terms of AD, once again unfortunately data are only subjective by means of Breast-Q and not objective regarding CC. I added in the text/references the aforementioned paper from Casella D to further increase data on the denervation topic. Moreover I changed the expression “definitive solution”, which actually would have needed a solid data background, with “promising” and “encouraging” . I also added a short paragraph to better explain the rationale of this procedure.

Changes in the text: LINE 40... Two recent studies coherently found that CC is

much higher in retro-pectoral cases rather than pre-pec ones (8,9). Nonetheless, cases of CC are described in pre-pec IBBRs as well, but often they are related to PMRT or previous radiation. When considering pre-pec cases only, PMRT makes the difference, as shown in an interesting article on this topic, published on this Journal (10), where CC is significantly different in pre-pec cases submitted to PMRT compared to those not submitted to it. Another study, once again published on this journal, showed a rate of CC in pre-pec IBBR cases followed by PMRT of 13.1% (11), suggesting that the adopted matrix played the key role. But, regarding this topic, Sinnott et al. (9) found that the contracture rates were three times higher in the retro-pectoral cases submitted to PMRT rather than the pre-pec ones equally submitted to PMRT. This result points out a quite easy hypothesis, that the muscle position coverage of the implant is the real difference and not the acellular dermal matrix use, as suggested by the aforementioned study by Graziano et al. (11). At this regard, the aforementioned study of Sobti (8) clearly states: “we found that the difference in capsular contracture rates among position of implant groups was statistically significant”. Indeed, So, it seems that the lower rates of CC in pre-pec cases are due to the absence of muscle over the implant rather than to the use of ADMs, also because similar low rates of CC in pre-pec cases have been described using synthetic meshes as well, even in the setting of PMRT (12,13). Moreover, RT effect in the CC rate of pre-pec cases is maintained even in the setting of pre-mastectomy RT (14). Thus, it seems that there are two main factors involved in the CC process, namely RT and the implant position. But, since a radiation-related fibrosis leading to a condition of CC of pre-pec cases is sometimes seen in pre-pec cases too, no matter which mesh is adopted, is mostly induced by RT, either pre- or post-mastectomy, . So, maybe, we could possibly argue that this is a particular type of fibrosis and a peculiar type of CC, which could be preferably considered as a separate entity, according to a specific paper on this issue (15). As a matter of fact, the majority On the other hand, there are a lot of CCs are not related to RT, once again with a striking prevalence in the retro-pectoral cases, as reported by a recent meta-analysis (16), showing that the muscle must be an independent key factor. and the type of fibrosis of a standard CC, not occurring after related to PMRT, is usually more a thickening of the capsule itself. Moreover, to clearly highlight the key-role of the muscle in the standard CC, there are always is most often another drawback accompanying CC, two “bad companions” such as “the animation deformity” and “the window shutter effect”. These two bad “guys” are This phenomenon is never described or seen in a pre-pectoral reconstruction. LINE 60...-21). LINE 67... allows an immediate and definitive promising solution with a rewarding feeling for the patient and surgeon together. LINE 69... In conclusion, in the tough choice of the “capsular contracture dilemma” there are two important clues:

the pre-pec IBBR long-term impressive result in terms of low rates of CC and the pectoralis major muscle denervation as an encouraging approach definitive resolution of to prevent and treat long-standing CC and for the avoidance of animation deformities. AFTER LINE 68 ... The rationale of such a procedure relies in avoiding the detrimental effect of the muscular constant movement over the implant. In fact, once the muscle has been detached from its sternal and costal attachments, its functionality becomes definitively compromised, while its viability is still essential to keep a vascularized cushion over the implant. Therefore a denervation, obtained by means of selective neurotomies (17), maintains the muscle viable while paralyzing it. Obviously an atrophy will follow and will lessen the thickness of the muscle itself to reduce it almost to an autologous biological matrix.

Reviewer B

Comment 1: It seems to be the 'on' of title is misspelling.

Reply 1: yes, thanks for pointing it out. I corrected “on” with “or”.

Changes in the text: LINE 1... “TO USE OR NOT TO USE THE MUSCLE”...

Comment 2: Is 'the window shutter effect' an official term?

Reply 2: thanks for your observation, actually is quite an informal term, which doesn't appear in the literature. In the past “window shading” has been seldom used (Namnoum JD. Expander/implant reconstruction with AlloDerm: recent experience. *Plast Reconstr Surg.* 2009 Aug;124(2):387-394. doi: 10.1097/PRS.0b013e3181aee95b). Besides, a “window shutter effect” is mostly a colorful expression to describe what happens in case of an initial animation deformity. Hence, since it is just part of of the animation deformity process, I removed this expression from the text in order to avoid confusion and neologism in this field.

Changes in the text: LINE 52... Moreover, to clearly highlight the key-role of the muscle in the standard CC, there are always is most often another drawback accompanying CC, two “bad companions” such as “the animation deformity” and “the window shutter effect”. These two bad “guys” are This phenomenon is never described or seen in a pre-pectoral reconstruction. LINE 55... deformities and window shutter effects, the standard CC we are often facing in IBBR could be due... LINE 64... aforementioned animation deformities and window shutter effects.

Comment 3: Can you elaborate on why two “bad companions” occur in subpectoral breast reconstruction?

Reply 3: I referred to animation deformity and window shutter effect as the “two bad companions” (and “bad guys”) that accompany the retro-pectoral standard IBBR, but,

as said above, the neologism of “window shutter effect” can be easily avoided. That’s why in the text I removed this two colloquial expressions too.

Changes in the text: LINE 52... Moreover, to clearly highlight the key-role of the muscle in the standard CC, there are always is most often another drawback accompanying CC, two “bad companions” such as “the animation deformity” and “the window shutter effect”. These two bad “guys” are This phenomenon is never described or seen in a pre-pectoral reconstruction.

Reviewer C: Thank you for the opportunity to review this editorial that describes a potential explanation for the cause of capsular contracture in implant-based breast reconstruction. I believe this editorial is based on the article published in this journal by Graziano et al. Given the lower rate of capsular contracture in prepectoral versus subpectoral implant-based breast reconstruction, the author argues that the position of the implant behind the pectoralis major muscle and the ensuing shearing forces between the implant and the muscle are the major causes of capsular contracture. The author also maintains that radiation-induced capsular contracture can be due to a radiation-related fibrosis and can be seen as a separate entity compared to standard capsular contracture which is not related to radiation therapy and is more of a thickening of the capsule. Furthermore, the author maintains that denervation of the pectoralis major muscle in subpectoral implant-based breast reconstruction may corroborate this theory and potentially mitigate the risk of capsular contracture. In this article the author provides some interesting insights on implant-based breast reconstruction and the origin of capsular contracture; however, there are a few points that require further clarification:

Comment 1: The position of the implant behind the pectoralis muscle and the shearing forces between the muscle and the implant can’t be the only cause of capsular contracture since it is seen in both prepectoral and subpectoral reconstructions, although at a lower rate in prepectoral reconstructions, and in non-radiated prepectoral reconstructions as well. There is not enough evidence to support the hypothesis that the positioning of the implant behind the pectoralis major muscle is the main culprit in capsular contracture in implant-based breast reconstruction. The cause of capsular contracture is most likely multifactorial and the shearing forces accompanying a retropectoral implant may be an element contributing to its development.

Reply 1: thanks indeed for your thorough review, done with great expertise and commitment. Yes my hypothesis is definitely a hint like a “stone in the pond”, suggesting what I believe might be the prevalent cause in a multifactorial and

complex phenomenon. The CC seen in case of PMRT, as clearly stated, is a phenomenon that involves both pre-pec and retro-pec cases and has peculiar histopathological features. On the other hand I have to admit that CC occurs in pre-pec cases without PMRT as well. But I still believe that a mechanical shearing force, albeit much inferior, is still the driving cause of this phenomenon, which is then maintained by many other factors to be identified case by case. Of course the editorial, once again, wants to be a starting point for a discussion on a novel perspective. I tried to clarify my point a little better in the text, adding a sentence of shearing forces in pre-pec cases too and mitigating my position by stating that there are certain others factors that contribute to a still quite unknown process.

Changes in the text: LINE 56... This process entails a constant shearing force, between the implant and the muscle, which is obviously higher in a retro-pectoral IBBR, where the force comes from above the implant with a constant crushing effect, rather than in a pre-pec setting. Nonetheless, a shearing force is obviously present in pre-pec IBBRs as well, since the mesh covering the implant, which will become the capsule, is always secured and fixed to the muscle, thus receiving a thrust from behind, anytime the muscle contracts and giving a slight movement to the implant even if it is placed in front of it. This might explain the very low CC rate in pre-pec patients in the absence of PMRT. Anyhow, there must be some other factor, in a multifactorial process, to explain why some patients develop CC while the majority don't.

Comment 2: The author states that radiation-induced capsular contracture may be due to a radiation-related fibrosis and be seen as a separate entity compared to standard capsular contracture which is more of a thickening of the capsule. This is an interesting viewpoint based on experience; however, in practice capsular contracture due to radiation therapy is not seen as a separate entity and is grouped together with other causes of capsular contracture and managed similarly. This idea should be supported with more evidence from the literature. If possible, it would be interesting to provide data on the severity or Baker grade of capsular contracture between radiated and non-radiated prepectoral or subpectoral reconstructions. Another study recently published showed that the rate of capsular contracture in non-radiated prepectoral implant reconstructions was 3.2% versus 19.7% in patients who received postmastectomy radiation therapy.² Unfortunately, the authors did not compare the Baker grade severity of capsular contracture between radiated and non-radiated groups.

Reply 2: well this is absolutely the point !!! There are a lot of studies that coherently present the same outcome: CC is higher in retro-pec IBBR than in pre-pec cases

(Sobti N, Weitzman RE, Nealon KP et al. Evaluation of capsular contracture following immediate prepectoral versus subpectoral direct-to-implant breast reconstruction. *Sci Rep.* 2020 Jan 24;10(1):1137. doi: 10.1038/s41598-020-58094-4), and when considering only the group of pre-pec cases, PMRT induces a higher rate of CC, in a statistically significant way (Polotto S, Bergamini ML, Pedrazzi G et al . One-step prepectoral breast reconstruction with porcine dermal matrix-covered implant: a protective technique improving the outcome in post-mastectomy radiation therapy setting. *Gland Surg.* 2020 Apr;9(2):219-228. doi: 10.21037/gs.2020.01.16.). I know very well the study you cited, which I added to my references (Sinnott CJ, Pronovost MT, Persing SM et al. The Impact of Premastectomy Versus Postmastectomy Radiation Therapy on Outcomes in Prepectoral Implant-Based Breast Reconstruction. *Ann Plast Surg.* 2021 Mar 18. doi: 10.1097/SAP.0000000000002801. Online ahead of print. PMID: 33833185), showing how RT effects on CC is induced even in case of pre-mastectomy RT in pre-pec cases. This is the basis of my statement that CC in the setting of PMRT has to be related to a very specific process, which is corroborated from an histopathological point of view by the study I cited in the text (14) and by a study from my own group that has been recently accepted for publication in *Bioactive Materials* and that describes CC in pre-pec cases with and without PMRT also by means of some pathological analysis of capsule samples (if I will have the chance to publish the present paper I will cite the ref of such study as soon as I get it from the Journal). On the other hand, there are many cases of CC in the absence of PMRT, with still a great prevalence in the retropectoral cases, according to a recent meta-analysis (Li Y, Xu G, Yu N et al. Prepectoral Versus Subpectoral Implant-Based Breast Reconstruction: A Meta-analysis. *Ann Plast Surg.* 2020 Oct;85(4):437-447. doi: 10.1097/SAP.0000000000002190). Hence, in such cases the implant position, or in other words the muscle use, is the key point. In this sense, I believe there are two entities of CC, one induced only by PMRT and the majority induced by the muscle with or without PMRT. But, as you clearly pointed out, there is a huge problem, namely the criterion, usually the Baker grade, on which a CC is deemed so. Most studies consider CC a complication when it is grade III and grade IV, but many of them don't even talk about grades. This could also explain why sometimes there's such a difference in the reported percentages of CC. And, last but not least, how can you objectively measure a CC Baker grade in a reproducible way from surgeon to surgeon? I expressed this important issue in the text quite clearly, but added a comment to make it clearer, according to your observations. Moreover, as per the issue of the specific PMRT related fibrosis and the role of the muscle, I made significant changes of the specific paragraph, to add 4 more literature refs, as you

correctly suggested, and to better explain my point of view.

Changes in the text: LINE 31 ... All these rates are, by the way, are flawed by the grade of Baker scale that is considered the threshold for CC (the vast majority of Authors consider only grade III and IV, but sometimes the adopted criterion is not reported, making a literature review very difficult), and mostly by the fact that such rating is always depending dependent on the visiting surgeon and not objectively measurable. LINE 40... Two recent studies coherently found that CC is much higher in retro-pectoral cases rather than pre-pec ones (8,9). Nonetheless, cases of CC are described in pre-pec IBBRs as well, but often they are related to PMRT or previous radiation. When considering pre-pec cases only, PMRT makes the difference, as shown in an interesting article on this topic, published on this Journal (10), where CC is significantly different in pre-pec cases submitted to PMRT compared to those not submitted to it. Another study, once again published on this journal, showed a rate of CC in pre-pec IBBR cases followed by PMRT of 13.1% (11), suggesting that the adopted matrix played the key role. But, regarding this topic, Sinnott et al. (9) found that the contracture rates were three times higher in the retro-pectoral cases submitted to PMRT rather than the pre-pec ones equally submitted to PMRT. This result points out a quite easy hypothesis, that the muscle position coverage of the implant is the real difference and not the acellular dermal matrix use, as suggested by the aforementioned study by Graziano et al. (11). At this regard, the aforementioned study of Sobti (8) clearly states: “we found that the difference in capsular contracture rates among position of implant groups was statistically significant”. Indeed, So, it seems that the lower rates of CC in pre-pec cases are due to the absence of muscle over the implant rather than to the use of ADMs, also because similar low rates of CC in pre-pec cases have been described using synthetic meshes as well, even in the setting of PMRT (12,13). Moreover, RT effect in the CC rate of pre-pec cases is maintained even in the setting of pre-mastectomy RT (14). Thus, it seems that there are two main factors involved in the CC process, namely RT and the implant position. But, since a radiation-related fibrosis leading to a condition of CC of pre-pec cases is sometimes seen in pre-pec cases too, no matter which mesh is adopted, is mostly induced by RT, either pre- or post-mastectomy, . So, maybe, we could possibly argue that this is a particular type of fibrosis and a peculiar type of CC, which could be preferably considered as a separate entity, according to a specific paper on this issue (15). As a matter of fact, the majority On the other hand, there are a lot of CCs are not related to RT, once again with a striking prevalence in the retro-pectoral cases, as reported by a recent meta-analysis (16), showing that the muscle must be an independent key factor. and the type of fibrosis of a standard CC, not occurring after related to PMRT, is usually more a thickening of the capsule itself. Moreover, to clearly highlight the key-

role of the muscle in the standard CC, there are always is most often another drawback accompanying CC, two “bad companions” such as “the animation deformity” and “the window shutter effect”. These two bad “guys” are This phenomenon is never described or seen in a pre-pectoral reconstruction.

Comment 3: The author states that, “As a matter of fact, the majority of capsular contractures are not related to radiation therapy, and the type of fibrosis of a standard CC, not related to RT, is usually more of a thickening of the capsule itself. The author should provide evidence to support this viewpoint that may not be shared by other experts in the field. The data in both Sinnott et al. manuscripts show that radiation therapy is a major cause of capsular contracture in prepectoral and subpectoral reconstruction.

Reply 3: as stated before, my personal point of view, which can obviously not be shared by others, is that there are two main causes and variables in the CC process, RT and the muscle use. CC is significantly higher in PMRT pre-pec cases in the study by Palotto, which I cited in the revision. And since pre-pec cases have usually a very low rate of CC, PMRT must be the main cause in this setting, with a specific fibrotic process, which is present even in the pre-mastectomy setting, according to the study by Sinnott you mentioned. Although, PMRT increases the rate of CC in retro-pec cases as well as reported by Sinnott in another study. But even adopting PMRT equally, retro-pec cases still have a much higher CC rate. Plus, the rate of CC is much higher in retro-pec cases compared to pre-pec ones even in the absence of PMRT, as reported in a very big meta-analysis by Li. Thus follows the deduction implied in my hypothesis, which is shared by Sobti, that the muscle must be a key player in this process. I mentioned one study that identifies some peculiar histopathological features of PMRT induced CC (14), and I hope to have the chance to cite my own paper with specific analysis on this, as soon as I’ll get the ref from the Journal. I think that the changes of the entire paragraph might help in clarifying this issue, add some literature data. Moreover, I changed the sentence you cited, “As a matter of fact, the majority of capsular contractures are not related to radiation therapy, and the type of fibrosis of a standard CC, not related to RT, is usually more of a thickening of the capsule itself”, rephrasing it in order to be less confusing avoiding “standard CC ... thickening of the capsule”, and in order to better clarify my two-different factor hypothesis, where the muscle is the second but decisive culprit.

Changes in the text: LINE 40... Two recent studies coherently found that CC is much higher in retro-pectoral cases rather than pre-pec ones (8,9). Nonetheless, cases of CC are described in pre-pec IBBRs as well, but often they are related to PMRT or previous radiation. When considering pre-pec cases only, PMRT makes the difference,

as shown in an interesting article on this topic, published on this Journal (10), where CC is significantly different in pre-pec cases submitted to PMRT compared to those not submitted to it. Another study, once again published on this journal, showed a rate of CC in pre-pec IBBR cases followed by PMRT of 13.1% (11), suggesting that the adopted matrix played the key role. But, regarding this topic, Sinnott et al. (9) found that the contracture rates were three times higher in the retro-pectoral cases submitted to PMRT rather than the pre-pec ones equally submitted to PMRT. This result points out a quite easy hypothesis, that the muscle position coverage of the implant is the real difference and not the acellular dermal matrix use, as suggested by the aforementioned study by Graziano et al. (11). At this regard, the aforementioned study of Sobti (8) clearly states: “we found that the difference in capsular contracture rates among position of implant groups was statistically significant”. Indeed, So, it seems that the lower rates of CC in pre-pec cases are due to the absence of muscle over the implant rather than to the use of ADMs, also because similar low rates of CC in pre-pec cases have been described using synthetic meshes as well, even in the setting of PMRT (12,13). Moreover, RT effect in the CC rate of pre-pec cases is maintained even in the setting of pre-mastectomy RT (14). Thus, it seems that there are two main factors involved in the CC process, namely RT and the implant position. But, since a radiation-related fibrosis leading to a condition of CC of pre-pec cases is sometimes seen in pre-pec cases too, no matter which mesh is adopted, is mostly induced by RT, either pre- or post-mastectomy, . So, maybe, we could possibly argue that this is a particular type of fibrosis and a peculiar type of CC, which could be preferably considered as a separate entity, according to a specific paper on this issue (15). As a matter of fact, the majority On the other hand, there are a lot of CCs are not related to RT, once again with a striking prevalence in the retro-pectoral cases, as reported by a recent meta-analysis (16), showing that the muscle must be an independent key factor. and the type of fibrosis of a standard CC, not occurring after related to PMRT, is usually more a thickening of the capsule itself. Moreover, to clearly highlight the key-role of the muscle in the standard CC, there are always is most often another drawback accompanying CC, two “bad companions” such as “the animation deformity” and “the window shutter effect”. These two bad “guys” are This phenomenon is never described or seen in a pre-pectoral reconstruction.

Comment 4: The author states, “Moreover, in the standard capsular contracture there are always two ‘bad companions,’ such as, ‘the animation deformity’ and the ‘window shutter effect.’ These two ‘bad guys’ are never described in prepectoral reconstruction.” Animation deformity and “window shading” are possible complications of subpectoral implant reconstruction and are not specific to capsular

contracture.

Reply 4: yes absolutely, animation deformity and window shading can be present even in the absence of CC, but the majority of CCs in retro-pec cases have these phenomena as well ! And this finding corroborates the idea that the muscle is a key player as shared in the study by Sobti (8). I removed “bad companions” and “bad guys”, in order to be less colloquial and confusing. Plus, as said before, I modified the text removing the “standard” word, and “window shutter effect”, which is seldom used and rarely in the literature (where I found only “window shading” as you wrote [Namnoum JD. Expander/implant reconstruction with AlloDerm: recent experience. *Plast Reconstr Surg.* 2009 Aug;124(2):387-394. doi: 10.1097/PRS.0b013e3181aee95b]). Thus, I left only the “animation deformity” definition, since “window shading” is just part of it. I rephrased the sentence to explain that such a phenomenon is commonly accompanying CC in retro-pec cases, but not being specific indicator of it.

Changes in the text: LINE 51... and the type of fibrosis of a standard CC, not occurring after related to PMRT, is usually more a thickening of the capsule itself. LINE 52... Moreover, to clearly highlight the key-role of the muscle in the standard CC, there are always is most often another drawback accompanying CC, two “bad companions” such as “the animation deformity” and “the window shutter effect”. These two bad “guys” are This phenomenon is never described or seen in a pre-pectoral reconstruction. LINE 55... deformities and window shutter effects, the standard CC we are often facing in IBBR could be due... LINE 64... aforementioned animation deformities and window shutter effects.

Comment 5: The author states, “Another suggestion that might corroborate this hypothesis is related to the novel technical modification, which I personally described on this Journal in 2017 and which has been reported by other Authors as well afterwards. This is the denervation of the pectoralis major muscle in case of a retropectoral approach.” To support the hypothesis that the subpectoral placement of implant and the ensuing shearing forces is the main culprit in the development of capsular contracture it should be shown that the capsular contracture rate is lower after this procedure. Also, denervating the pectoralis major muscle to preemptively reduce the rate of potential capsular contracture seems overly aggressive since the pectoralis major muscle is used not only in strenuous exercise but also in activities of daily living.

Reply 5: of course definitive data on long term CC evaluation after selective pectoralis major muscle denervation would be essential. An objective evaluation on CC is still missing and right now it is only a hint to move in the direction I believe

might be the solution, namely preventing muscular contractions. In the first study on this novel technique, which I published (17), there is a series of 56 procedures with patient-reported subjective evaluation. I have another article in press with 50 more patients, but still with a subjective evaluation by means of Breast-Q (the Covid restrictions on F-UP in the last year at our Institution stopped me from an objective evaluation on the CC rate in this cohort, being a non necessary outpatient visit). Moreover, there is a very recent paper of a former colleague of mine, Casella D, who reported a series of 62 patients submitted to pectoralis major muscle denervation with very good results in terms of AD, once again unfortunately data are only subjective by means of Breast-Q and not objective regarding CC. I added in the text/references the aforementioned paper from Casella D to further increase data on the denervation topic. Moreover I changed the expression “definitive solution”, which actually would have needed a solid data background, with “promising” and “encouraging”. As for your comment about the aggressiveness of denervating the pec muscle, I must disagree regarding its usefulness in a woman submitted to IBBR. Once the muscle is detached, as it has to be (keeping intact only its fascia) from the sternum and ribs, its functionality is no more helpful apart from the clavicular bundle, which remains intact and not denervated in the selective technique I introduced (17). Thus its movement is only transmitted to the capsule and no more to the chest wall, which is easily seen during its contraction maneuver. The pectoralis minor muscle and the clavicular bundle of the major took the place and do all the job ! I added a paragraph to better explain the rationale of the selective denervation, I described in my previous paper, and my point.

Changes in the text: LINE 60...-21). LINE 67... allows an immediate and definitive promising solution with a rewarding feeling for the patient and surgeon together. LINE 69... In conclusion, in the tough choice of the “capsular contracture dilemma” there are two important clues: the pre-pec IBBR long-term impressive result in terms of low rates of CC and the pectoralis major muscle denervation as an encouraging approach definitive resolution of to prevent and treat long-standing CC and for the avoidance of animation deformities. AFTER LINE 68 ... The rationale of such a procedure relies in avoiding the detrimental effect of the muscular constant movement over the implant. In fact, once the muscle has been detached from its sternal and costal attachments, its functionality becomes definitively compromised, while its viability is still essential to keep a vascularized cushion over the implant. Therefore a denervation, obtained by means of selective neurotomies, maintains the muscle viable while paralyzing its lower two thirds, the sternal and costal bundles (17). Obviously an atrophy will follow and will lessen the thickness of the muscle itself to reduce it almost to an autologous biological matrix.

Comment 6: There are a few sentences that require grammatical revision:

- a. The first sentence of the article should be written as follows, “Breast surgery is now facing an era of implant-based breast reconstruction (IBBR).”
- b. The second sentence could be written as follows, “In Europe, IBBR is the most common choice after conservative mastectomy, sometimes comprising more than 90% of the breast reconstructions performed.”
- c. The sentence on line 31 should read, “All these rates, are by the way, flawed by the grade of Baker scale that is considered the threshold for CC and mostly by the fact that such rating is always dependent on the visiting surgeon and not objectively measurable.”
- d. The sentence on line 34 should read, “None of them, by the way, has ever been eventually identified as the “one.”

Reply 6: thanks indeed for your grammatical corrections, which I obviously adopted in the text.

Changes in the text: ^[SEP]LINE 1...Breast Surgery is now facing the an era of Implant Based Breast Reconstructions (IBBRs) LINE 1... In Europe IBBR is the most common choice in case of a conservative mastectomy, sometimes comprising more than 90% of the breast reconstructions performed (1). LINE 31... All these rates are, by the way, are flawed by the grade of Baker scale that is considered the threshold for CC (the vast majority of Authors consider only grade III and IV, but sometimes the adopted criterion is not reported, making a literature review very difficult), and mostly by the fact that such rating is always depending dependent on the visiting surgeon and not objectively measurable. LINE 34... None of them, by the way, has never been eventually identified as the “one”.

Comment 7: The author uses metaphors throughout the manuscript to support and express their ideas (ie, “pleasure cruise,” “culprit,” “bad companions,” “bad guys,” “impeach the real felon,” etc). The use of gendered metaphors (ie, “bad guys”) should be avoided as it promotes gender inequality. The use metaphors and political metaphors should be minimized in scientific writing since they can sometimes confuse the reader, undermine the objectives of the study and reinforce stereotypes.

Reply 7: ...I removed “bad companions,” “bad guys,” “impeach the real felon,” to follow your suggestion.

Changes in the text: LINE 52... Moreover, to clearly highlight the key-role of the muscle in the standard CC, there are always is most often another drawback accompanying CC, two “bad companions” such as “the animation deformity” and “the window shutter effect”. These two bad “guys” are This phenomenon is never

described or seen in a pre-pectoral reconstruction. LINE 71... We could, hence, say that we are almost close to impeach identify the real felon reason that causes CC...

Comment 8: The author did not follow the instructions for authors regarding the formatting for the References. For each citation the first three authors should be listed followed by et al. for the remaining authors.

References 1. Graziano FD, Shay PL, Sanati-Mehrzy P, et al. Prepectoral implant reconstruction in the setting of post-mastectomy radiation. *Gland Surg.* Jan;10(1):411-416. Doi: 10.21037/g.s.2020.03.33.

References 2. Sinnott CJ, Pronovost MT, Persing SM, et al. The impact of premastectomy versus postmastectomy radiation therapy on outcomes in prepectoral implant-based breast reconstruction. *Ann Plast Surg.* 2021 Mar 18. Doi: 10.1097/SAP.0000000000002801.

Reply 8: Yes you are right, I didn't apply the right format to refs, so I changed all of them according to the Journal instructions.

Changes in the text: REFERENCES (1) Casella D, Calabrese C, Orzalesi L et al. Current trends and outcomes of breast reconstruction following nipple-sparing mastectomy: results from a national multicentric registry with 1006 cases over a 6-year period. *Breast Cancer.* 2017 May;24(3):451-457. doi: 10.1007/s12282-016-0726-z

(2) American Society of Plastic Surgeons Statistics. Available at: <https://www.plasticsurgery.org/documents/News/Statistics/2019/plastic-surgery-statistics-full-report-2019.pdf>

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