



# The Impact of SARS-CoV-2 Vaccination and Infection on Soft Tissue Fillers

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### Introduction

Despite the current low number of reported cases, reactions caused by mRNA vaccinations to SARS-CoV-2 in patients with pre-existing filler is a cause of concern to all aesthetic practitioners. It is well established in the literature, that Delayed Onset Nodules (DONs) or Delayed Onset Reactions (DORs) can occur weeks, months or even years after receiving a soft tissue filler treatment when the immune system is challenged. Potential triggers include viral illnesses<sup>1</sup>, bacterial infections (most commonly sinus, ear, or dental infections), dental procedures<sup>2</sup>, excessive UV exposure, subsequent minimally invasive aesthetic treatments, and vaccinations<sup>3</sup>. mRNA vaccinations are known to be highly immunogenic<sup>4</sup> by increasing protein translation and modulating innate and adaptive immunogenicity, so it is no surprise that they are also capable of activating an immune response in foreign body implants. However, a study of 106 participants from 18 different countries concluded that COVID-19 vaccines did not appear to confer a greater risk of a soft tissue reaction than other identified triggers<sup>5</sup>.

Similarly, acute infection with COVID-19 can also profoundly stimulate the immune system and create a DON or a DOR in a patient who has previously undergone a filler treatment. Current case studies suggest that these reactions are more protracted and can be more difficult to resolve.

Regarding soft tissue swelling following COVID-19 vaccination, this is not unique to these vaccines and similar reactions can occur to many different vaccinations<sup>6</sup>. However, the

cohort of patients that regularly receive vaccinations, such as the annual influenza vaccine, are generally different to the cohort of patients that undergo soft tissue filler procedures and as the COVID-19 vaccination is currently targeting the entire adult population, the incidence of soft tissue filler reactions is likely to rise.

### Mechanism

It is known that the spike protein of SARS-CoV-2 enters cells by binding and blockade of the angiotensin 2 receptors (ACE2) thus creating a pro-inflammatory response and a proliferation of T cells. A study by Li et al (2020)<sup>7</sup> demonstrated that the skin has moderately high levels of ACE2 proteins in the basal layer of the epidermis and also lining the vasculature which may provide the mechanism to why soft tissue fillers may react in an adverse manner. It is also known that delayed hypersensitivity reactions tend to be T cell mediated rather than due to a B cell antibody response<sup>1</sup>.

### Incidence

There are currently few published cases that demonstrate a DON or a DOR following either the COVID-19 vaccination or infection. Although due to lockdown restrictions and the current global vaccination programme, these numbers are expected to rise once the number of procedures performed escalate to pre-pandemic levels. It is essential that all practitioners are mindful of this risk, consent their patients appropriately, risk assess their patients, carefully time their treatments around their expected vaccination date and are knowledgeable on how and when to intervene if a complication does occur.

## Signs and Symptoms

An international consensus group described delayed inflammatory reactions manifesting as discolouration (mostly erythema), painful nodules, induration, tissue hardening and solid oedema<sup>8</sup>. Munavalli et al (2021)<sup>9</sup> who reported on 4 specific cases relevant to this topic included symptoms of significant swelling, burning sensation of the lips, erythema, and tenderness. The oedema appeared to coincide with areas of previous filler injections in all cases.

## Areas of caution

Although the data is currently extremely limited, the provisional evidence would suggest that the tear trough, malar and perioral regions are most susceptible to DORs<sup>9</sup> following COVID-19 infection or vaccination, but this may just represent the greater frequency that these areas are treated. However, patients that have had lip filler or tear trough treatments in the last 6-12 months should be considered at a higher risk.

## Minimising the risk

Before performing any soft tissue filler treatment, the practitioner must take a full medical history, including previous and recent COVID-19 infection and vaccination schedule. Soft tissue filler augmentation is an elective procedure performed by aesthetic practitioners and, as such, should not interfere with patients who are scheduled to undergo SARS-CoV-2 vaccination<sup>3</sup>.

The data from the Moderna vaccine trial highlighted two cases of facial swelling and one case of angioderma in patients who had previously had soft tissue fillers in these areas. One had treatment within 2 weeks, one within 6 months and one unreported. Given the study population of 15,184 patients and the incidence of facial filler treatments, it is likely that a significant number of these patients would have had treatment within the last 12 months. For this reason, the ACE Group

considers the reaction within 2 weeks of receiving treatment to be significant. Although current evidence is limited, the ACE Group recommend that soft tissue filler augmentation should not be performed on any patient who is due to receive a mRNA vaccination within 2 weeks following treatment. At the time of writing, there are no documented cases of DONs or DORs with the non-replicating adenovirus vaccination that is used for the Oxford/AstraZeneca COVID-19 vaccination but would also advice caution and allow a timescale of 2 weeks prior to vaccination for performing soft tissue augmentation.

From studies on other vaccinations, it is known that the immune response from administration to developing an antibody response that the first 3 weeks are pivotal, and this is when the immune system is most stimulated. Data from Israel in a population of 500,000 has provided further evidence. Following the Pfizer vaccine, immunity within the first 2 weeks of administration remained almost at zero but then rose to about 90% at 3 weeks and then did not rise any further<sup>10</sup>. For this reason, the ACE Group recommends that soft tissue filler treatments are not performed within 3 weeks of receiving a vaccine. This guidance would apply to all current COVID-19 vaccinations.

Although all the current SARS-CoV-2 vaccinations do not use live virus for their immunogenicity, any patient who is immunocompromised by virtue of a medical condition, medication or undergoing oncological treatment should be considered a high-risk. Individual risk assessment based on their medical history should occur, in consultation with their specialist, where appropriate.

Previous soft tissue filler treatments are not a contra-indication to vaccination and these patients should be encouraged to be vaccinated but advised to contact their healthcare practitioner if they do develop some facial swelling following the vaccine<sup>11</sup>.

## Consent

Although the incidence is very low, it is important that patients are fully aware of any risks related to COVID-19 infection or vaccination and soft tissue fillers. The ACE Group emphasises that this should be included on consent forms:

Although there is limited evidence and only a very small number of cases, there is a risk of inflammatory reactions and soft tissue swelling in patients who have previously had soft tissue fillers, or plan to have treatment, after receiving COVID-19 vaccination.

Do not undergo soft tissue filler procedures within 2 weeks of your planned vaccination date or within 3 weeks having received it.

Do not attend for treatment if you have symptoms consistent with COVID-19 or are suffering from ongoing symptoms from previous infection.

If you develop any reactions following your treatment, it is imperative you contact your healthcare practitioner at the earliest opportunity.

If you develop any reactions following your treatment, you may require medication to manage the complication. This may include oral steroid medication which may lower your immunity to COVID-19 if you have recently been vaccinated.

## Treatment of DONs and DORs caused by COVID-19 vaccination

The current evidence would suggest that acute DORs in patients with soft tissue fillers presents as mild to moderate oedema, which is sometimes associated with erythema and tenderness, although cases of angioedema have also been reported. These reactions are often spontaneous and self-limiting<sup>3</sup> and are likely to be due to the heightened immune

response following the vaccination but quickly subside without treatment. However, if the response is greater than expected or lasts more than a few days, the evidence suggests that a short course of corticosteroids<sup>3</sup> is likely to manage the complication quickly. The ACE Group recommends a dose of 40mg oral Prednisolone for a duration of 5 days. As an alternative, Dexamethasone 5mg orally for 3 days can be used. Dexamethasone has a longer half-life of 36-72 hours (compared to prednisolone which has a half-life of 18-36 hours).

There are concerns between the medical society and patients that the administration of oral corticosteroids may affect mounting an effective immune response to SARS-CoV-2. The prescribing practitioner must consider the seriousness of the DOR and the individual's medical history before issuing any medication. Immune response is based on many criteria including age, health, lifestyle factors, medical history, and concomitant medication.

Doses of Prednisolone above 20mg per day (or 2mg/kg) for 2 or more weeks or more are sufficiently immunosuppressive to warrant concerns about live vaccinations<sup>12</sup>, however steroid therapies that are short term (less than 2 weeks), alternative day, physiological replacement or topical/aerosol are not contraindications. Although, the response to vaccines may be suboptimal.

If the DON or DOR that occurs because of COVID-19 vaccination does not respond as expected, practitioners should follow the guidelines for COVID-19 infection.

## Treatment of DONs and DORs caused by COVID-19 infection

It would initially be prudent to treat the acute inflammatory response the same as treating the reaction to a SARS-CoV-2 vaccination as this may resolve the situation in a swift and uncomplicated manner. However, from the limited evidence available, patients who contract COVID-19 and develop a DON or DOR

tend to have a more recalcitrant problem needing multiple interventions.

If there is minimal response to an initial course of oral corticosteroids, or the problem escalates, the ACE Group recommends a prescription of a tetracycline (such as Doxycycline 100mg BD or Minocycline 100mg BD)<sup>13</sup>. These agents not only have antibiotic properties but also anti-inflammatory and anti-humoral activity. If the patient is allergic to tetracyclines or there are other contraindications, a macrolide (such as Clarithromycin 500mg BD) should be considered. Response to treatment should be assessed and dual therapy considered.

Depending on response, hyaluronidase should be considered for hyaluronic acid dermal fillers whilst remaining on antibiotic cover. The dosage used will depend on the extent and size of nodules and the filler product used, but will usually be between 500 to 1000 units, injected directly into the nodules to infiltrate and disperse them and at multiple depths and angles of injection. Follow up and assessment must be undertaken, and hyaluronidase may be repeated up to three times at suitable intervals.

For cases failing to respond or for non-hyaluronic acid fillers, there is evidence for the injection of intralesional steroids (such as triamcinolone acetonide or methylprednisolone acetate) and anti-mitotic agents (such as 5-fluorouracil)<sup>13</sup>. These drugs should be used at a suitable concentration and volume and gradually increased according to response. The ACE Group recommends that only practitioners familiar with these agents and competent at managing complications should consider these treatments and less experienced practitioners should refer.

## **Angiotensin Converting Enzyme Inhibitors (ACE Inhibitors)**

Due to the mechanism of action of the SARS-CoV-2 virus penetrating cell membranes by accessing the ACE2 receptor mechanism, research has been conducted into the use of

ACE inhibitors and ARB (Angiotensin II Receptor Blockers) in the treatment of COVID-19 and its complications. The single case report in the aesthetics journals, whereby a single case responded quickly (likely spontaneous resolution based on the timescale), the ACE Group cannot recommend this as a potential treatment at this time.

## **Anti-Histamines**

The mechanism of immune response following a DON or a DOR is likely to be a Type IV delayed hypersensitivity reaction, mediated by a T-lymphocyte response. However, even though Type IV immunogenic reactions are unresponsive to anti-histamines<sup>14</sup>, there have been reported cases of improvement following the administration of anti-histamines<sup>6</sup>. Due to the low risk of adverse events related to the prescribing of anti-histamines and the small, but possible, risk of advantageous outcomes, the ACE Group suggests consideration of the use of an oral anti-histamine in the case of a recalcitrant DON or DOR following COVID-19 infection or vaccination.

## **Other Aesthetic Procedures**

There is currently no evidence that COVID-19 vaccination or infection has a detrimental effect on other aesthetic procedures, including botulinum toxin. However, as patients may become unwell and experience flu-like symptoms following vaccination, the ACE Group recommends avoiding treatments for 1 week post vaccine.

## **Reporting**

There is a distinct lack of reporting of complications in aesthetic practice. The ACE Group advocates that all practitioners should report complications to the manufacturers and the MHRA. The ACE Group also provides a reporting mechanism to facilitate this process via the website and App. Due to the lack of evidence concerning COVID-19 vaccine and infection, it is even more important that reporting occurs. The MHRA have created a

dedicated Coronavirus Yellow Card reporting site which should be used:

<https://coronavirus-yellowcard.mhra.gov.uk/>

### **Key Points:**

1. Acute soft tissue reactions following mRNA vaccination, including oedema, erythema, and tenderness, appear to be very low in number, relatively mild and self-limiting. Adopting a watchful waiting approach may be the sensible option, especially as treating with oral corticosteroids may impair the immune response to the vaccine.
2. More severe, acute reactions, such as angioedema, should be managed according to the severity although a short course of moderate to high dose corticosteroids, with or without anti-histamines, is likely to bring a speedy resolution to the problem.
3. Considering this evidence, patients need to understand the potential risks of soft tissue filler treatments around vaccinations and infections and this should be part of the screening and consent process.

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