It is always interesting to discuss which reconstitution volumes various aesthetic practitioners prefer for their botulinum toxins (BoNTAs). The dilution volume varies widely. Some injectors prefer to be more dilute with more bacteriostatic normal saline (NaCl) for a larger diffusion in certain areas, such as underarms, and to be more concentrated with use of smaller reconstitution amounts for more precise administration of the BoNTA, such as glabellar lines. Some practitioners believe dilution volumes don't matter at all in relation to spread or diffusion. It can get confusing when there is more than one injector in an office who may be using different volumes of NaCl for dilution and, additionally, may be using more than one type of syringe to administer the neurotoxin. This type of scenario may allow for greater confusion and subsequent dosage errors (Black et al., 2012).

The terminology used to describe the movement of BoNTA varies in the literature and this can also be perplexing. Cliff et al. (2008) described the local movement as “migration”; while Pickett et al. (2008) used the terms “diffusion and migration”; and Walker et al. (2003) preferred the term “local spread.” Ramirez-
Castaneda et al. (2013), are even more specific: they differentiated the local physical movement as “spread,” the more microscopic movement of the molecules by passive transport as “diffusion” and used the term “migration” for distant spread. Finally, regulatory authorities use the terms “diffusion,” “regional diffusion,” or “local spread” when referring to local effects in contiguous muscles and “distant spread” for non-contiguous areas (Brin et al., 2014).

How can we simplify and prevent dosage errors? The ability to provide consistency of desired outcomes with BoNTA is key to retaining patients and fostering trust.

1. **Have a meeting with all injectors in the office and decide which standard dilution to use so it is always mixed with the same dilution.**

2. **The standard reconstitution volume can be increased for that individual patient just before the injection.**

3. **Figure out which syringes you will need for that particular NaCl volume. Syringes should be chosen so that each hash mark equals one unit.**

4. **Chart which reconstitution volume you use each and every time for consistency.**

**Step 1: Choose a Standard Reconstitution Volume.** This can be a tough go in some offices. Sometimes people are resistant to change because they have done it that way for years. Consistency will go a long way to reduce dosage errors, so it is important to decide this standard reconstitution volume first (Black et al., 2012). Our office uses a 2 ml standard for 100 U Botox, and 100 Xeomin and 2 ml standard for 300 U Dysport because we believe this is an optimal concentration for most areas of the face when placed in the muscles correctly. Many offices I visit use a 1 ml standard for the three types mentioned above. This provides more flexibility when one wants very little diffusion, and it is easy to add NaCl when desired. We have chosen not to change to the 1 ml because we have not had any issues with too much diffusion and we are happy with the results we've seen with the 2 ml reconstitution.

**Step 2: Just Before Injection, Increase Dilution Volume for Specific Areas.** For those of us not gifted in math this can get confusing. Below is my dilution table for Botox. It also works for Xeomin. A Dysport vial would need a different table because it is has 300 units per vial. Remember that brands of BoNTA have different measurements for units and they are not interchangeable.
Here's an example of how I use this reconstitution table nearly every day: Jane is getting her glabella and her peri-oral lines injected. I would like a 2 ml NaCl dilution for her glabella but prefer a 4 ml dilution for her peri-oral lines so that my 5 units can diffuse fairly evenly over her entire upper lip. I would first draw up my NaCl because I wouldn’t want to accidentally put Botox in my NaCl by drawing Botox up first. I do some simple subtraction first. I would like 5 units for Jane's obicularis oris muscle. I know that 4 ml dilution would require 0.2 ml NaCl. I also know that with my standard dilution of 2 ml I would need 0.1 ml to get my 5 unit dose. 0.2 minus 0.1 is 0.1. Thus, I add another 0.1 NaCl first, then go to my Botox vial for the additional 0.1 (5 units). Now I have 5 units with a 4 ml reconstitution volume.

Perhaps Jane also would like her underarms injected for her hyperhidrosis. I would like to have a 4 ml dilution for a greater diffusion. If a 50 unit dose is required for each underarm area, I know I’ll want 2 ml per armpit. I also know my standard dilution of 2 ml would require 1 ml for 50 units. 2-1=1. I would first draw up 1 ml NaCl then add another 1 ml of my standard Botox solution.
Step 3: Choose Your Syringe. This is fun. My favorite syringes for BoNTA are BD insulin syringes because the needles are swedged-on, needing no hub or additional needles. There is absolutely no waste. I would like to point out that I use a lot of BD syringes because the tiny 31 G and 32 G needles dull with just a few pokes. I tend to draw up one syringe for each area, and this can mean 5-6 syringes per patient. Luckily, BD syringes are rather inexpensive. I also use a specialized tool called a Kebby Decapper to take the metal ring off of the vial. A standard bottle opener can work, but it can also break or chip the glass vial.

After I remove the metal ring I take the vial off carefully in an aseptic manner so I don't dull the needle by putting it through the tough rubber stopper. I also take special care not to touch the needle to the glass of the vial. The needles dull very easily because they are so fine. I also take the rubber stopper off of the bacteriostatic NaCl to modify my reconstitution volume when using BD insulin syringes.

Syringes: Which syringes/dilutions allow dash to equal 1 Unit?

For those who prefer 1 ml dilution, BD insulin syringes with increments of "5 units" are great. These are 0.5 ml and 0.3 ml sizes. With this dilution, each little dash equals 1 unit. Dosages are super easy to deliver when each little line tells you how many units you are delivering. Each dash equals one unit. It is also convenient because each number reflects the amount of neurotoxin units.
For aesthetic injectors who prefer a 2 ml reconstitution volume, the best choice are BD insulin syringes with increments of "10 units". These syringes are 1 ml in size and each 10 units equals 0.1 ml. Don't let the "units" on the syringe fool you, each dash is still only 1 unit. Each "10 unit" increment is only 0.1 ml, or 5 units. I like to pretend there is a decimal before each number (.10, .20, etc.). Remember, these syringes were created for insulin units, not neurotoxin units. Each number on the syringe is not the correct number of units like the 1 ml dilution. The 10 on the syringe equals 5 units of neurotoxin, the 20 equals 10 units, and so on. Still, with this size, every dash is one unit.
There are other syringes that one could use. Some have a plunger to decrease waste of neurotoxin. An example of this is pictured below, the Braun Injekt syringe. The advantage of these is that you can draw up all of the intended units and change the needle when it is dull. One could also draw the BoNTA through the rubber stopper with a larger-bore needle first and change needle to a 31G or 32G needle before administering the neurotoxin.
For practitioners who prefer the on-label dilution of 2.5 ml, Unitox makes a syringe in which every line is one unit too.

**Step 4: Chart Dilutions Used.** This is important. Careful charting makes a difference because we want to repeat what works and fix what doesn’t. Whether your office utilizes EMR or paper charting, you can easily make a notation when you alter the standard reconstitution volume.

If you think of the tip of your needle as the bullseye of a target and think of the target size as the diffusion area, you can picture that a 1 ml target is rather small, a 2 ml target has a larger area, and a 4 ml target is going to have an even larger area. With experience, you'll be able to predict dilutions in your mind’s eye each time you place that needle in your patient’s muscle. The amount of units injected also directly effects the diffusion area.
Note: There is disagreement in the literature regarding the effect of dilution volume with efficacy. More clinical data is needed. A more concentrated solution such as 1 cc per 100 U may allow for less pain, more accurate placement, and it may decrease diffusion (Tremaine & McCullough, 2010). More dilute formulations have been shown to have a shorter duration of effect (Black et al., 2012). Hsu et al. conducted a study that showed dilution does impact efficacy and diffusion. Their findings indicated larger volumes of NaCl led to greater diffusion and showed the affected area was larger (Hsu et al., 2004). Other studies such as Hankins et al. (1998) argue that reconstitution volumes make no difference in efficacy or diffusion (Tremaine & McCullough, 2010).

I tend to agree with the Black et al. and the Hsu et al. school of thought. Since 2002 I have tried various dilution volumes in certain areas and have developed a preference for various areas. For example, I used to place 4-5 units of Botox in the superior orbicularis oris using the 2 ml/100U dilution. Patients frequently returned with a bird beak look when they puckered. I changed to the 4 ml/100U dilution and the results looked more uniform and smooth.

Finally, I would like to stress the importance of technique. Technique plays a big part in diffusion or spread. Studies show that spread is influenced by injection technique, speed of injection, dilution, needle size, dose, volume, and BoNTA
utilized (Ramirez-Castaneda et al., 2013). Researchers can measure spread or diffusion by measuring anhydrosis halo or “action halo” that utilizing the iodine-starch test. This test clearly shows that dose contributes to diffusion. These tests also highlight the fact that different BoNTAs are not interchangeable. Anhydrosis halo tests also show that volume and concentration play a part in diffusion and spread (Ramirez-Castaneda et al., 2013).

Please comment about dilution solutions you’ve found. I would love to hear from you, you can contact me through my website at www.DisappearingActLaser.com or you can email me at JBKaesthetics@gmail.com I look forward to hearing your thoughts, experiences, suggestions, and tips.

Thank you very much,

Julie Bass Kaplan MSN, RN, CPSN, CANS


Spread is a fast and active process and is directly related to amount of volume (though much larger than the differences described here), depth of injection, speed of injection and needle size. Diffusion is a slow and passive process as when the toxin moves to the receptors. The field of effect is influenced by the physical aspects at the time of injection and by dose after the injection. If you are injecting slowly and have correct placement, the field of effect is dose related as evidenced by the iodine-starch test done by Hexsel et al. 2012. Therefore, there is no reason to adjust reconstitution volumes for different areas, only dose.

It is all about technique. I agree changing dilution is less predictable and can be less effective.
Hi Karen, thank you for your thoughtful comments. You brought up some excellent points and this is a great topic for research and discussion. I will revise my post to be more clear and to stimulate thought about the points you raised.

There is certainly disagreement in the literature regarding the effect of dilution volume with efficacy. We need more clinical data. A more concentrated solution such as 1 cc per 100 U may allow for less pain, more accurate placement, and it may decrease diffusion (Tremaine & McCullough, 2010). More dilute formulations have been shown to have a shorter duration of effect (Black et al., 2012). Hsu et al. conducted a study that showed dilution does impact efficacy and diffusion. Their findings indicated larger volumes of NaCl led to greater diffusion and showed the affected area was larger (Hsu et al., 2004). Other studies such as Hankins et al. (1998) agree with your assertion that reconstitution volumes make no difference in efficacy or diffusion (Tremaine & McCullough, 2010).

I tend to agree with the Black et al. and the Hsu et al. school of thought. Since 2002 I have tried various dilution volumes in certain areas and have developed a preference for various areas. For example, I used to place 4-5 units of Botox in the superior orbicularis oris using the 2 ml/100U dilution. Patients frequently returned with a bird beak look when they puckered. I changed to the 4 ml/100U dilution and the results looked more uniform and smooth.

You also brought up a good point about terminology. Terminology for the movement of BoNTA varies in the literature. Cliff et al. (2008) described the local movement as "migration" while Pickett et al. (2008) used the terms "diffusion and migration." Walker et al. (2003) preferred the term "local spread" Ramirez-Castaneda et al. (2013) are even more specific. They differentiated the local physical movement as "spread," the more microscopic movement of the molecules by passive transport as "diffusion" and used the term "migration" for distant spread. Finally, regulatory authorities use the terms "diffusion, regional diffusion," or "local spread" when referring to local effects in contiguous muscles and "distant spread" for non-contiguous areas (Brin et al., 2014).

I agree with you that technique plays a big part in diffusion or spread. Studies show that spread is influenced by injection technique, speed of injection, dilution, needle size, dose, volume, and BoNTA utilized (Ramirez-Castaneda et al., 2013). The anhydrosis halo or "action halo" that you mention utilizing the iodine-starch test has been utilized by various researchers and like you said, clearly shows that dose contributes to diffusion. These tests also highlight the fact that different BoNTAs are not interchangeable. Anhydrosis halo tests also show that volume and concentration play a part in diffusion and spread (Ramirez-Castaneda et al., 2013).

Thank you again for your experience and insight. What a fascinating discussion. I will revise my post to be more consistent with the terms and will include references for my research. I really appreciate your comments. Thank you!!!

It will be fascinating to see what future studies on this topic show and it will also be interesting to see the BoNTA products of the future emerge. 😊

Thank you again, Julie