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#### INITIATOR

- 1. USU Principal Author/Presenter: Jones, Brandon CPT, DC
- 2. Academic Title: Dr/Senior Resident
- 3. School/DepartmenUCenter: Army Postgraduate Dental School, AEGD-2 Program, Fort Hood, TX
- 4. Phone: (708) 227-2152
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#### CHAIR OR DEPARTMENT HEAD APPROVAL

- 1. Name: Mark McClary, COL, DC, Director
- 2. School/Dept.: Army Postgraduate Dental School, AEGD-2 Program, Fort Hood, TX
- 3. Date: 1 May 2016
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- 1. Name: Michael E. Garvin, COL, DC, Commander
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1. Name: Thomas Schneid, Executive Dean
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# Volume of Anesthetic in 0.5% Marcaine with 1:200,000 Epinephrine Dental Carpule

#### A Thesis

Presented to the Faculty of the Advanced Education in General Dentistry, Two-Year Program,

United States Army Dental Activity, Fort Hood, Texas

And the Uniformed Services University of the Health Sciences – Post Graduate Dental College

In Partial Fulfillment of the Requirements for the Degree of

Master of Science in Oral Biology

Ву

Brandon Jones, CPT, USA, DC

April 2016

## Volume of Anesthetic in 0.5% Marcaine with 1:200,000 Epinephrine Dental Carpule

#### A REPORT ON

Research project to evaluate the actual volume of a 1.8 mL solution of 0.5% Marcaine with 1:200,000 epinephrine dental carpule for determination of maximum dose

By:

Brandon Jones, CPT, USA, DC

D.D.S, Marquette University School of Dentistry- 2012

Mentor Staffing By:

Zac Highberger, MAJ, USA, DC

D.M.D, University of Pittsburgh School of Dental Medicine-2004

Fort Hood, Texas

April 2016

#### ABSTRACT

**Purpose:** The purpose of this study is to evaluate the actual volume of a 1.8 mL solution of 0.5% Marcaine with 1:200,000 epinephrine dental carpule for determination of maximum dose.

Methods: Measurements of the total volume of anesthetic using 10 carpules of 0.5% Marcaine with 1:200,000 epinephrine from 3 different LOT numbers (n=30 carpules) was measured using a balance to capture the mass of each carpule (Total Mass). Once the total mass of the carpule was obtained, the anesthetic was emptied and the carpule was once again measured using a balance (mass of empty carpule). Mass (total)-mass (empty carpule) =mass of the anesthetic. After calculating the mass of the anesthetic, the investigator determined volume by using the equation density=mass/volume with density being a control value number of 1. The average and standard deviation of each LOT number was calculated and compared to the manufactures printed volume of 1.8 mL.

**Results:** The average and standard deviation were plotted as Fluid (g) vs LOT numbers, labeled as "Pilot (10 carpules/LOT)." The p value was calculated and found to be much greater than 0.05 (0.4496) indicating that there was no significant difference between them. By using a density of 1, our data reveals an approximate 0.05 increase in volume in comparison with the manufactures stated volume.

**Conclusion:** By using 1 as our control unit value for density, our results show and approximate 0.05 increases in volume compared to the manufactures printed volume of 1.8 mL. However, these results are only based on an approximation of the density as the manufacture could only state that the actual density is "very close to 1", without a more accurate measure.

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#### TABLE OF CONTENTS

Section	Page
Introduction	6
Purpose and Hypothesis	13
Materials and Methods	14
Results	19
Discussion	21
Conclusion	27
Bibliography	28

#### INTRODUCTION

The Army Dental Care System provides services on a daily basis for thousands of active duty men and women and, in some cases, their dependents. This fact alone requires that providers not only be competent, but efficient in their practice of dentistry. Efficiency in, dentistry often is referred to as reducing the amount of time patients are in the dental chair. Local anesthesia has provided a pathway to allow providers to treat patients efficiently, comfortably, and in a timely manner. Although local anesthetics are generally regarded as safe and effective, the amount of anesthetic used throughout a procedure can be easily overlooked if not understood properly. The intended purpose of this research is to equip providers with assurance in calculations of maximum dose of 0.5% Marcaine with 1:200,000 epinephrine and confidence that the carpule they use is in fact 1.8 mL. The relevance of this research will not be to prove efficacy or choice of anesthetic.

The history of local anesthetic often is dated back in 1859 with the successful isolation of cocaine by Niemann .¹ By 1884, cocaine was being used effectively for regional anesthesia during an oral surgery procedure performed by Halsted to extract a 3<sup>rd</sup> molar without pain. ² Due to the high mortality rates associated with cocaine, however, the first ester-type anesthetic procaine was synthesized in 1905 and was widely used for more than four decades.¹ Procaine lost support among dental providers because of its connection to high incidences of allergic reactions. In 1943, Lofgren synthesized the amide derivative anesthetic lidocaine, which is still the most commonly used anesthetic in dentistry worldwide.¹ Other notable local anesthetics

introduced to dentistry since Lofgren include (but are not limited to): mepivacaine 1957, prilocaine 1960, bupivacaine 1963, and articaine 1969.<sup>2</sup>

The dental cartridge is a single-use item of the dental professional's anesthesia armamentarium designed for use for one patient and then disposed of. <sup>3</sup> The dental cartridge is otherwise known as and referred to by dentists as a carpule. <sup>4</sup> The now routinely used term carpule was trademarked in 1920 by Cook-Waite Laboratories and will be the choice term used throughout this text. <sup>4</sup> The glass cylinder of a dental carpule contains the local anesthetic drug and other ingredients. Components of the carpule itself include: the glass cylinder, stopper, aluminum cap, and the diaphragm. The glass cylinder houses the anesthetic which is held in place at one end (which receives the harpoon from the aspirating syringe) by the silicone rubber stopper and the other end (which receives needle penetration) by the aluminum cap and diaphragm. In an intact dental carpule, the rubber stopper occupies a little less than 0.2 mL of the total volume of the entire carpule containing the local anesthetic and other ingredients. <sup>4</sup>

Local anesthetics must include: rapid onset of action, adequate duration of anesthesia, and substances (i.e local anesthetics, vasoconstrictors) with minimal or no systemic toxicity. Dental local anesthetic carpules typically contain the following ingredients: local anesthetic, vasopressor (if epinephrine or levonordefrin is included), antioxidant (if epinephrine or levonordefrin is included), sodium chloride, and distilled water. The local anesthetic is used to interrupt the propagated nerve impulse, preventing it from reaching the brain and causing pain. The vasopressor, if used, either epinephrine or levonordefrin, is added because of vasoconstrictive properties. Local anesthetics are vasodiolators; they eventually are absorbed

into the circulation, where their systemic effect is related directly to their blood plasma level. <sup>14</sup> Vasoconstriction at the site of the injection is beneficial because it limits the uptake of the anesthetic by the vasculature, thereby increasing the duration of the anesthetic and diminishing systemic effects. <sup>6</sup> If a vasopressor is added, then so will an antioxidant. The antioxidant most often used is sodium (meta) bisulfite. Oxygen can become trapped in the carpule during the manufacturing process or diffuse through the semipermeable diaphragm causing oxidation of the vasopressor. Sodium bisulfite negates this process and prevents oxidation of the vasopressor. <sup>4</sup> Sodium chloride is added to the carpule to make the solution isotonic with the tissues of the body. <sup>4</sup> Distilled water is used to add volume and to dilute the concentration <sup>4</sup>. Lastly, a small bubble of nitrogen gas of approximately 1 to 2mm in diameter is used to prevent oxygen from being trapped inside the cartridge, which potentially could destroy the vasopressor.<sup>4</sup>

Local anesthesia is a principle way of preventing pain and discomfort during dental treatment. <sup>7</sup> It is impossible to provide effective dental care without the use of local anesthetics. <sup>8</sup> All local anesthetics contain an aromatic ring linked to amide groups. The link is either an amide or ester and thus determines the classification. <sup>6</sup> The aromatic ring improves the lipid solubility of the compound, which in turn enhances the diffusion through nerve sheaths and neural membranes. <sup>8</sup> This property of lipid solubility refers to the concept known as potency.

Potency is one of three principle properties by which all local anesthetics can be evaluated; the other two are duration and onset. Potency as described earlier refers to lipid

solubility. Marcaine is a more potent local anesthetic than lidocaine. Therefore only a 0.5% solution is required to obtain comparable local anesthesia, instead of a 2% solution as seen with lidocaine. The degree of protein binding of a local anesthetic agent determines the duration of the anesthetic. A greater degree of protein binding at the receptor site will create a longer duration of action. Lastly, the onset of an anesthetic refers to the pKa. Pertaining to the local anesthetic solution, local anesthetics exist simultaneously as uncharged molecules (bases) and also as positively charged molecules (cations). This proportion of cations and bases becomes variable depending on the pH of surrounding tissues during a routine dental injection. The pKa is a measure of the affinity of a molecule for hydrogen ions; thus the lower the pka the more rapid the onset of action. This is due to the greater amount of base molecules present to diffuse through the nerve sheath and reduce the onset of action. Furthermore, the closer the pKa of the local anesthetic is to the pH of the tissue (7.4), the more rapid the onset.

Sodium channels exist normally in a resting state during which sodium ions are denied entry into neuronal membranes. When neuronal tissue becomes stimulated, the channel assumes an activated to an open state, in which sodium ions diffuse into the cell causing an action potential also known as a nerve impulse. Local anesthetics efficacy is often defined by their mechanism of action, which is their ability to bind to sodium channels receptors, leading to reduction or elimination of the permeability of theses ions and interruption of nervous conduction.

0.5% Marcaine (Bupivacaine) with 1:200,000 epinephrine, is one of many choices regarding the use local anesthetics. In a survey conducted in 2007 regarding types of

formulations of local anesthetics used by Ontario dentists, Marcaine was the least commonly used anesthetic compared to lidocaine, articaine, prilocaine, mepivacaine, and their specific formulations. <sup>9</sup> Marcaine has been FDA approved since 1972 and available in a carpule form since February 1982. <sup>4</sup> There are two primary indications for use of Marcaine in dentistry, lengthy dental procedures, and management of postoperative pain. <sup>4</sup> Due to its higher lipid solubility and higher degree of protein binding, Marcaine has a longer duration of action than lidocaine, which is the gold standard to which all new local anesthetics are compared. <sup>10</sup> In addition, the longer duration of action gives Marcaine a significant advantage managing postoperative pain especially when used with a nonsteroidal anti-inflammatory drugs (NSAID) post surgically. <sup>11,12,13</sup> Due to Marcaine's longer duration of action in comparison to other formulations of dental local anesthetics, it is generally recommended not to use Marcaine in pediatric, physically, or mentally disabled individuals. <sup>14</sup>

Local anesthetics are believed to be the most frequently used drugs in clinical dentistry. 

Although they are generally regarded as safe, some adverse reactions can occur if proper knowledge of their use is ignored. 

One particularly important aspect of their use is maximum recommended dose (MRD).

Adult Doses for Commonly Used Local Anesthetics in Dentistry

AGENT	CARPULE SIZE (mg)	mg/kg	mg/lb	MAXIMUM DOSE
2% Lidocaine	36	7	3.3	500
w/1:100k Epi				
3% Mepivacaine	54	5.5	2.6	400
4% Prilocaine w/	72	8	4	600
1:200k Epi				
0.5%	9	1.3	0.6	90
Bupivacaine				
w/1:200k Epi				
4% Articaine	68	7	3.2	500
w/1:100k Epi				

Maximum dosages are based on an adult weight of 150 lb or 70 kg. (Reference from Oral and Maxillofacial Surgery Secrets 2<sup>nd</sup> Edition)

Local anesthetic toxicity occurs when blood levels of the drug become too high, leading to cerebrovascular and cardiovascular complications. <sup>15</sup> Toxic effects are usually characterized by an excitatory and depressive phases, which may include the following: restlessness, anxiousness, confusion, tremors, convulsions, rapid pulse rate, increased blood pressure in the so called excitatory phase. However, the depressive phase would cause both blood pressure and pulse rate to drop leading to, unconsciousness, respiratory and/or cardiac arrest. <sup>16</sup>

Dr. Stanley F. Malamed, a renowned expert in the field of dental anesthesia and author of the *Handbook of Local Anesthesia*, wrote in depth about the importance of maximum dose regarding local anesthetics. In his latest edition book (6<sup>th</sup> edition), he makes a point regarding labeling changes of some dental carpules that indicate the volume of solution contained in the carpule is 1.7 mL, not the "traditional" 1.8 mL. Dental carpules did not always contain 1.8 mL. During the late 1990's, during the FDA approval process of Septocaine (Articaine), the question

was asked by the FDA, "Can you guarantee that each and every cartridge contains a least 1.8 mL of solution?". <sup>4</sup> The answer to this question was "No" due to slight mechanical variations during the filling process. However, when the manufactures were asked if they could guarantee that each and every cartridge contains at least 1.7 mL of solution, the answer was "Yes.". <sup>4</sup>

Through use of a standard syringe and a 27-gauge needle Robertson and collegues when performing a study regarding "The Anesthetic Efficacy of Articaine in Buccal Infiltration of Mandibular Posterior Teeth," deposited the contents of 50 Articaine carpules and 50 Lidocaine carpules into a graduated syringe with 0.01 milliliter increments divisions. <sup>17</sup> They found that even though Articaine labeled its carpule 1.7 mL and Lidocaine labeled its carpule 1.8 mL the actual expressed volume of anesthetic was found on average to be 1.76 mL. <sup>17,18</sup> Due to this finding, Malamed recommends using 1.8 mL as the volume of choice when calculating maximum dose. <sup>4</sup>

Considering this inconsistency of actual expressed volumes of anesthetic between Articaine and Lidocaine, the primary purpose of this study will be to evaluate the actual volume of a 1.8 mL solution of 0.5% Marcaine with 1:200,000 epinephrine dental carpule for determination of maximum dose.

#### <u>PURPOSE</u>

The purpose of this study is to evaluate the actual volume of a 1.8 mL solution of 0.5% Marcaine with 1:200,000 epinephrine dental carpule for determination of maximum dose.

#### **HYPOTHESIS**

Null hypothesis is no statistically significant difference in volumes of anesthetics per dental carpule of 0.5% Marcaine with 1:200,000 of epinephrine; thus no change to calculation of maximum dose indicated.

#### MATERIALS AND METHODS

Thirty carpules (n=30) of Marcaine (Bupivacaine) 0.5% with epinephrine 1:200,000 were used throughout the study. All carpules were manufactured by the Cook-Waite Laboratories for CARESTREAM HEALTH INC. Three separate LOT numbers were used with ten carpules from each LOT. LOT numbers included in the study were: LOT# D01070A, LOT# D01066A, and LOT# D01009A. All carpules were inspected prior to the study and evaluated for any defects and or imperfections deeming them unfit for use during the study.

The volume of each carpule was calculated over the course of two days at the Carl R.

Darnall Army Medical Center Pathology Laboratory. The mass of each carpule was collected using a Mettler Toledo Analytical Scale measuring out in grams to the ten-thousandths place (4 decimal places) (Figure 1). Data was gathered and then recorded using an Excel spreadsheet.

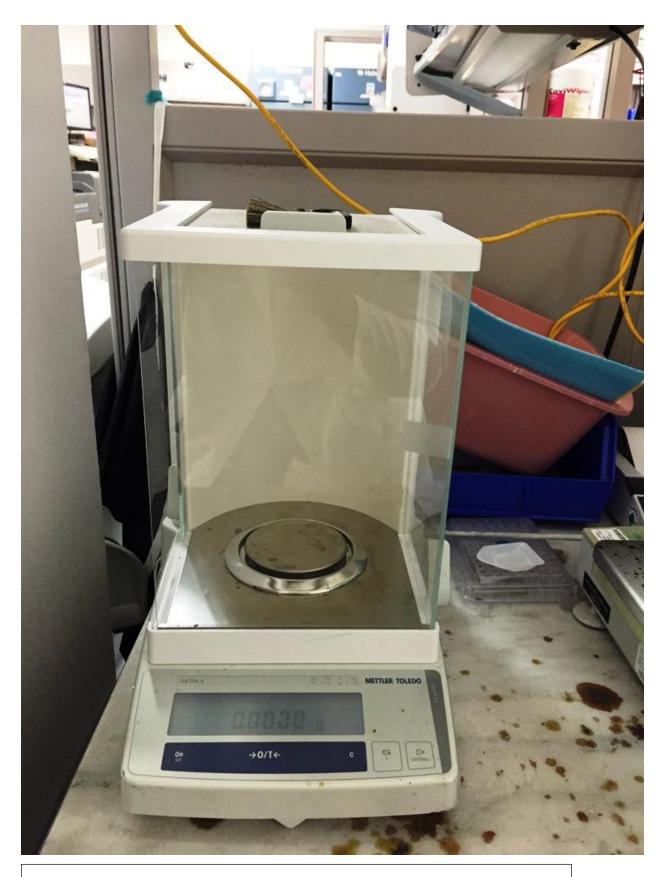
Volume was later calculated using the density equation D=m/v with density being a controlled standard value of 1.

The study design was separated in half with (n=15) carpules five from each LOT number on the first day and (n=15) five from each LOT number on the second day for a total number of thirty carpules (n=30) tested. Prior to the use of the analytical scale, the scale was "zeroed" and ensured the screen read all zeros up to four decimal places (Figure 1). Each carpule was weighed on the scale to obtain the Mass of a Full Carpule (Figure 2). The contents of the carpule were then deposited into a plastic cup using an aspirating dental syringe and a 27- gauge long needle. The rubber stopper was then slowly retracted backwards using the harpoon of the syringe. The harpoon was never dislodged from the rubber stopper. Completely removing the

harpoon from the stopper, made it difficult to reengage, which prevented the stopper from totally being removed from the glass cylinder. All carpules whose harpoons were completely removed from stopper were discarded from the study.

Once the rubber stopper was completely removed from glass cylinder, residual anesthetic inside cylinder was also removed using a combination of a cotton-tip applicator and 2x2 cotton gauze. The rubber stopper was then reinserted back into the glass cylinder and the mass of empty carpule was then taken using the analytical scale (Figure 3). Both masses of the full and empty carpules were plotted on an Excel spreadsheet (Figure 3). Lastly, the mass of the anesthetic was also plotted by first subtracting the mass of (full) carpule minus the mass of the (empty) carpule and labeled as (fluid) on the spreadsheet (Figure 3).

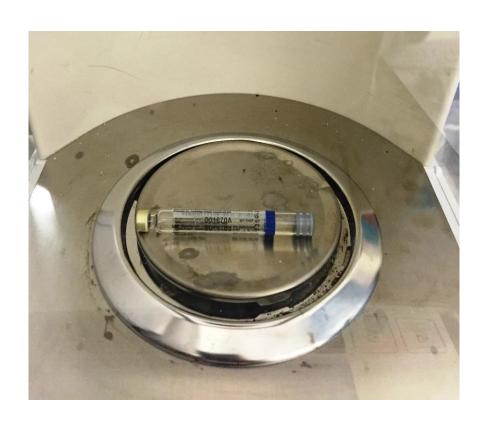
The volume of each carpule from each LOT number was calculated using the density formula D=m/v where D=density m=mass and v=volume. By using 1 as the control value number for density, the volume was assessed to equal the mass of the anesthetic v=m. This final volume recorded as the (fluid) column on the spreadsheet (Figure 4).



**FIGURE 1:** *Mettler Toledo Analytical Scale* 



**FIGURE 2:** *Mass of full carpule* 



## **FIGURE 3:** *Mass of empty carpule*

## **FIGURE 4:** Fluid volume spreadsheet

	Unit (Gram)					
LOT#	Sample Full Empty Fluid					
<u>D01070A</u>						
	1	5.6130	3.7503	1.8627		
	2	5.6267	3.7684	1.8583		
	3	5.6249	3.7671	1.8578		
	4	5.6200	3.7847	1.8353		
	5	5.6217	3.7562	1.8655		
	6	5.6144	3.7499	1.8645		
	7	5.5624	3.7236	1.8388		
	8	5.6982	3.8091	1.8891		
	9	5.6081	3.7517	1.8564		
	10	5.5804	3.7666	1.8138		
<u>LOT#</u> <u>D01066A</u>	Sample	Full	Empty	Fluid		
<u>D01000A</u>	1	5.6107	3.7578	1.8529		
	2	5.6506	3.7813	1.8693		
	3	5.5972	3.7395	1.8577		
	4	5.6259	3.7566	1.8693		
	5	5.6100	3.7506	1.8594		
	6	5.6488	3.7713	1.8775		
	7	5.6295	3.7745	1.855		
	8	5.6282	3.7645	1.8637		
	9	5.637	3.7869	1.8501		
	10	5.6356	3.7606	1.875		
LOT# D01009A	Sample	Full	Empty	Fluid		
	1	5.6640	3.7927	1.8713		
	2	5.6466	3.7764	1.8702		
	3	5.6406	3.7854	1.8552		
	4	5.6837	3.8122	1.8715		
	5	5.6034	3.7618	1.8416		
	6	5.6621	3.8072	1.8549		
	7	5.6085	3.7708	1.8377		
	8	5.6282	3.7746	1.8536		
	9	5.6928	3.8158	1.877		
	10	5.5979	3.7565	1.8414		

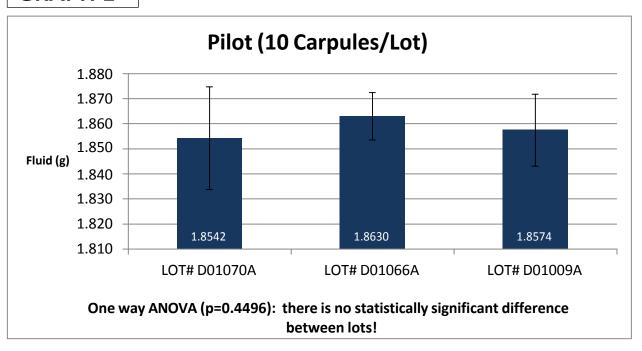
#### RESULTS

The average and standard deviation is presented using table 1 and the graph 1 below. A One-way ANOVA test was used to calculate the p value of 0.4496 shown in table 2. Because the p value was much greater than 0.05, the null hypothesis was accepted, and there is no statistically significant difference between LOTS.

#### **TABLE 1**

	Unit (Gram)					
	LOT# D01070A	LOT# D01066A	LOT# D01009A			
Average	1.8542	1.8630	1.8574			
SD	0.0205	0.0095	0.0144			

#### **GRAPH 1**



## TABLE 2

Oneway Analysis of Flu	id By Lot						
Oneway Anova							
Summary of Fit							
Rsquare	0.057498						
Adj Rsquare	-0.01232						
Root Mean Square Error	0.015458						
Mean of Response	1.858217						
Observations (or Sum Wgts)	30						
Analysis of Variance							
Source	DF	Sum of Squares	Mean Square	F Ratio	Prob >		
Lot	2	0.00039361	0.000197	0.8236	0.4496	Not significant!	
Error	27	0.00645203	0.000239				
C. Total	29	0.00684564					
Means for Oneway Anova							
Level	Number	Mean	Std Error	Lower 95%	Upper 95%		
LOT# D01009A	10	1.85744	0.00489	1.8474	1.8675		
LOT# D01066A	10	1.86299	0.00489	1.853	1.873		
LOT# D01070A	10	1.85422	0.00489	1.8442	1.8643		
Std Error uses a							
pooled estimate of error variance							

#### **DISCUSSION**

Local anesthetics have unparalleled pharmacological use in dentistry. Thus, dental professionals must have a special awareness of how these medications are dosed. This point is emphasized by Becker and Reed, who emphasize that "The use of anesthetic cartridges in dentistry has unfortunately spawned carelessness in appreciating the actual amount of anesthetic we administer to our patient". <sup>19</sup> They go on to highlight the idea that a dental carpule represents a volume, not a dose that is more properly expressed as milligrams or micrograms. <sup>19</sup> These conclusions support a consensus in the field to simplify dosage calculations of dental carpules and to use 2 mL of volume instead of the printed 1.7 or 1.8 mL. This recommendation correlates with the proposal made by Malamed in his 6<sup>th</sup> edition of his handbook, where he suggests the usage of 1.8 mL for all dental local anesthetics. <sup>4</sup>These concepts relate to the idea that it is always better to overestimate rather than underestimate leading to a safe model of practice.

The results of this study concluded that, among three different LOT numbers of 0.5% Marcaine with 1:200,000 of epinephrine, there were no statistically significant different volumes between them. The study also found that the average volumes were as follows: LOT D01070A (1.8542 mL), LOT D01066A (1.8630 mL), and LOT D01009A (1.8574 mL). These averages are all higher than the printed volume of 1.8 mL the manufacture states on the carpule and package insert. There are several reasons for these results.

Prior to the initiation of the study, and during the review of the literature, the exact density of Marcaine was researched online through the Material Safety Data Sheet (MSDS)

from Cook-Waite laboratories. After reviewing the MSDS, it was clear that the exact density of Marcaine was not published. Final efforts were made to contact the manufacture directly (Cook-Waite Laboratories). After speaking with the manufacturing department, the representative could be no more exact than saying that the density is "very close to 1".

Density is defined as the mass of a substance per unit of volume. <sup>20</sup> Its formula is depicted as D=m/v where m=mass and v=volume. This equation is of particular importance regarding this study as its use was needed in calculation of the volume of each carpule of Marcaine. Because the manufacture could only disclose that the density is "very close to 1," the consensus was made to use 1 as the density value throughout the study. By using 1 as the standard value for density, the volume of the anesthetic was found to equal the mass in grams through solving for "v" in the density equation. This conclusion, however, has some inherent problems.

The choice to use 1 as the density value for this study was made based on the chemical composition of Marcaine. According to the MSDS sheet produced by Carestream Health Inc., the chemical composition of Marcaine is mostly liquid water which has a density of approximately 1.0 g/mL.<sup>21</sup> SEE TABLE 2 BELOW

**TABLE 2:** Marcaine Composition Information Regarding Ingrediants

Chemical Name	CAS-No	Weight %	Trade
			Secret
Water	7732-18-5	98-100	*
7732-18-5			
Sodium chloride	7647-14-5	<1	*
7647-14-5			
Bupivacaine	18010-40-7	<1	*
hydrochloride			
18010-40-7			
Sodium	7681-57-4	<0.1	*
metabisulfite			
7681-57-4			

<sup>\*</sup>The exact percentages (concentrations) have been withheld as trade secrets. (Reference from Carestream Material and Safety Data Sheet regarding Marcaine 2012-05-16)

Temperature and pressure are two units of particular importance regarding a volumetric study. Temperature affects water molecules directly: water takes up more space as temperature increases. For example, we can compare the density of water at 25 degrees

Celsius to water at 80 degrees Celsius. The density decreases from 0.9970g/ml to 0.9718 as it is heated. The same is true in the opposite direction liquid water at 25 degrees Celsius 0.9970 g/ml to liquid water at 4 degrees Celsius 0.99997 g/mL. Density increases as the temperature decreases. Changes in pressure have very little effect on the volume of a liquid. Liquids are relatively incompressible because any increase in pressure can only slightly reduce the distance between the closely packed molecules.

In order to be absolutely accurate regarding the actual volume of anesthetic of each carpule, it is imperative to know the exact temperature and pressure at which the carpules were manufactured. This information could then be used to replicate those conditions in the

study. However, the exact temperature and pressure at which the carpules were manufactured is unknown. Furthermore, the exact temperature and pressure at which this study was conducted is also unknown. A calculation of exact volume of the fluid is dependent on the temperature and pressure at which the measurement of the fluid was is obtained.

There are several unknowns here: one, we do not know the manufacture's density for each carpule; two, we don't know the temperature and pressure at which each carpule was made; and, three, the temperature and pressure at which we used to make the measurements may not match the temperature and pressure of fabrication. All this will create errors in our final fluid volume data; this error can be as big as 0.05 mL of volume if we were to assume a density of 1.

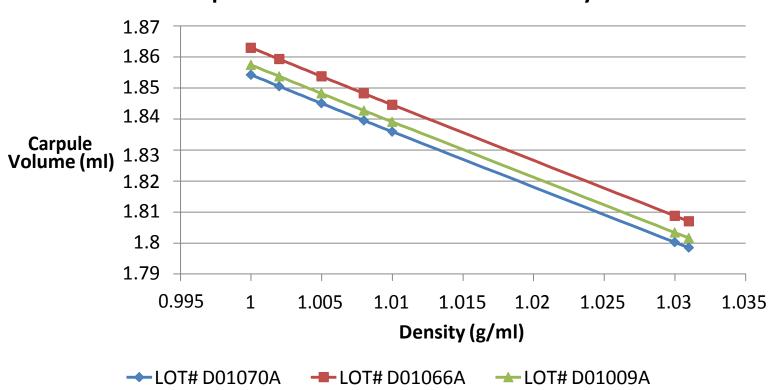
Though these uncertainties exist, we can predict the carpule volume at a specific density by plotting the carpule volume as a function of various densities. SEE GRAPH 2/TABLE 3 BELOW. For example, if we are to assume a density of 1.031 g/ml, our carpule volume would be ~1.80 ml; this is very close to manufactures stated volume. On the other hand, if we were to use the density of 1, our carpule volume is ~ 1.85 ml; this shows a ~0.05 increases in volume in comparison with the manufactures stated volume.

**TABLE 3:** Volume of Marcaine as a function of various densities

		D	ensity (g/ml)					
	P	1	1.002	1.005	1.008	1.01	1.03	1.0
	verage							
	(gram)							
<u>LOT</u>	1	. 1	1.850	1.844	1.839	1.835	1.800	1.7
<u>D01070A</u>	.8542	.85422	518962	995025	503968	861386	213592	467507
<u>LOT</u>	1	. 1	1.859	1.853	1.848	1.844	1.808	1.8
D01066A	.8630	.86299	271457	721393	204365	544554	728155	973812
LOT	1	. 1	1.853	1.848	1.842	1.839	1.803	1.8
D01009A	.8574	.85744	732535	199005	698413	049505	339806	590689

**GRAPH 2** 





The observation noted by Robertson and colleagues regarding the average volume of 1.76 mL of anesthetic for Septocaine and Lidocaine demonstrates a worthwhile comparison to this research design. In their design protocol, they used a dental syringe to express the volume of anesthetic into a graduated cylinder marked with 0.01 mL increments. This differs from our design protocol, which adds the additional step of removing the rubber stopper and drying out completely the internal aspect of the glass cylinder prior to measuring out the final mass. This added step ensures the complete removal of anesthetic for a more accurate determination of the mass and furthermore the volume of anesthetic; however, the question could be asked, which method has greater clinical validity?

Roberson and colleagues note that a small amount of anesthetic solution remained in both carpules after delivery. <sup>18</sup> During a routine dental injection of a full carpule of anesthetic, the clinician usually terminates the injection after the rubber stopper hits the opposite end of the glass cylinder; thus reinforcing the observation that a small amount could remain in the cylinder. In addition, not otherwise noted by Robertson and colleagues, there could also be a small amount of anesthetic that remains in the lumen of the needle as well.

Roberson and colleagues used a graduated cylinder to take their measurements of expressed volume of anesthetic, in comparison to the use of an analytical scale in our research design to determine mass. This difference in protocol may offer more accurate final results by relying on a calibrated balance rather than visual observations.

#### CONCLUSION

Although the average volume of 0.5% Marcaine with 1:200,000 epinephrine varied slightly between the three different LOT numbers used in this study, the difference was not found to be statistically significant. Due to these findings, the null hypothesis of there is no statistically significant difference in volumes of anesthetics per dental carpule of 0.5% Marcaine with 1:200,000 of epinephrine will be accepted and no recommendation for change or alteration in maximum recommend dose regarding Marcaine dental carpules will be suggested at this time. However, further investigation regarding the exact density and physical conditions at which Marcaine is manufactured may produce even more accurate results regarding whether or not the actual volume is in fact 1.8 mL.

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