International Journal of Science and Engineering Applications
Volume 9 - Issue 06, 87 - 90, 2020, ISSN:- 2319 - 7560

Metal Filled Carbon Nanotubes for Targeted Radiation Therapy: A Feasibility Study

S. Ashmeg	M. Rodriguez	D. Gregory	A. Parbatani	E. Eienbraun
SUNY Polytechnic Institute	SUNY Polytechnic Institute	SUNY Polytechnic Institute	SUNY Polytechnic Institute	SUNY Polytechnic Institute
Albany, NY 1220	Albany, NY 1220	Albany, NY 1220	Albany, NY 1220	Albany, NY 1220

Abstract: This research involves demonstrating the viability of filling the nanotubes with copper and characterizing its effectiveness as a vehicle for transport of radionuclide. A two-step filling method has been adopted in this study. First, the multi-walled carbon nanotubes (MWCNTs) closed ends were opened by acid reflux; then, using the capillary effect, the tubes were filled with copper by sonicating them in a copper salt solution. The effects of changing the reflux time, changing the molar concentration and replacing the copper nitrate salt with copper chloride have been studied. The success of this process has been tested using scanning electron microscopy (SEM), energy dispersive x-ray spectroscopy (EDS), x-ray photoelectron spectroscopy (XPS) and transmission electron microscopy (TEM). Using a 12 hour reflux time in 68% HNO_3 resulted in opening of the MWCNTs which in turn allowed filling them with copper. The filling took place by sonicating the opened MWCNTs in 0.87 mol/L $Cu(NO_3)_2$ solution. Subsequent characterization by EDS and XPS show the presence of copper in the MWCNTs. Variations in reflux time and copper molar concentration were observed to change the copper concentration. TEM images show that the Cu nanoparticles are located inside the nanotubes.
Multi-walled carbon nanotubes were reproducibly filled with copper using a $Cu(NO_3)_2$ solution. Altering the reflux time and the copper molar concentration were shown to affect the subsequent copper concentrations in the MWCNTs. These data form a proof of concept supporting the ability to use MWCNTs filled with copper for targeted radiotherapy.
Keywords: CNTs, MWCNTs, Carbon Nanotubes, Radiotherapy, Targeted Therapy.

1. INTRODUCTION

Carbon nanotubes (CNTs) are known for their unique physical and chemical properties. CNTs can be single-walled or multi-walled, and can possess a range of chiralities, diameters, and lengths, all of which affect the character of the CNT [1]. Nano-carriers, including carbon nanotubes, are being extensively studied for use in cancer diagnostics and therapies. In comparison to other Nano-carriers, CNTs have superior flow dynamics and better cell permeability due to their needle-like shape [2,3,4,5]. In addition, they can be shortened and functionalized to decrease toxicity [5,6,7]. Both the insides and outsides of the tubes can be utilized to carry treatment and targeting agents simultaneously. Consequently, carbon nanotubes have been the focus of many in-vitro and in-vivo studies where they serve to carry bio-functional agents [2, 3, 4, 5, 6].

The filling of carbon nanotubes with metallic nanoparticles is an established procedure in many fields and there are several methods to fill the CNTs whether using melted solids or salt solutions [7,8]. The solution method is chosen here to minimize the risk of radiation hazard, the alternative would require melting a radioactive material.

Cu^{67} is a radioactive copper isotope that primarily decays via beta emission with a half-life of 2.6 days to Zn^{67}. The average range of the emitted beta particle is 5 mm in water, which makes this source suitable for small tumors with minimal shielding concerns[9]. This work describes a study to determine the feasibility of filling carbon nanotubes with copper as a first step to be used in targeted radiotherapy.

2. MATERIALS AND METHODS

The process for filling MWCNTs was done in two steps: first, opening the MWCNTs, followed by impregnating the MWCNTs with copper.

To open the MWCNTs, the tubes are stirred and refluxed in 68% nitric acid at 120°C for times between 12 and 24 hours. When refluxing, the MWCNTs and the acid are combined in a flask, with a magnetic rod for stirring. This process functionalizes the tubes and breaks the carbon-carbon double bonds at the CNT ends. After reflux, the tubes are washed with deionized (DI) water until pH-neutral. Then the wet tubes are left in an oven at 65°C for at least 24 hours to dry.

After the tubes are dried, they are sonicated in 0.87 mol/L $Cu(NO_3)_2$ solution for 30 minutes followed by DI water wash and sonication in DI water for another 30 minutes. The filled and washed MWCNTs are left to dry and samples are then prepared for analysis. Sample preparation is done by dropping filled MWCNTs sonicated for one minute in ethanol on 1x1 cm^2 pieces of Si, or onto a copper grid for TEM analysis. For SEM and EDS analyses, the Si samples were mounted on stubs using double sided carbon tape to secure them. Samples for XPS analyses were mounted directly on the removable stage using copper pins to secure the samples.

For copper filling analysis, SEM and TEM images were collected along with EDS and XPS spectra. A Zeiss LEO 1550 SEM (Zeiss, Oberkochen, Germany), with a field emission source was used. The sample is bombarded with 3-5 keV electrons. As those electrons strike the sample, secondary electrons leave and get collected by an in-lens detector located in the same column as the electron gun. For EDS, the SEM system is used but the stage is dropped down to around 15mm away from the pole piece and the accelerating voltage is increased to > 10 kV. The x-rays from the sample are detected by a Bruker x-ray detector mounted on the SEM tool.

For XPS analyses, a ThetaProbe (Thermo Fisher Scientific, Waltham, MA) x-ray photoelectric spectroscope was used. The x-rays in the XPS tool are produced from an aluminum source then filtered by a crystal resulting in a monochromatic Kα x-ray beam (1486.6 eV) striking the sample. The analysis area is 100 micrometers in diameter which is poor lateral resolution for nanomaterials. However, the data is collected from the first few nanometers from the surface giving a superior depth resolution when compared to EDS. In addition, XPS shows the chemical forms of the elements present in the sample. Combining the two spectroscopes provides sufficient data to support existence of Cu in the samples.

For transmission electron microscopy (TEM), a JEOL 2010 was used (JEOL, Tokyo, Japan). In TEM, the electrons are accelerated by an applied high voltage (200kV) and travel across a thin sample to provide a contrasted image based on the atomic number of the material.

3. RESULTS

3.1 Imaging of filled MWCNTs

Figure 1 represents SEM images of a sample with copper filled MWCNTs. The images of all the samples look similar, including the ones of unfilled MWCNTs. Therefore, more data from different modalities had to be acquired.

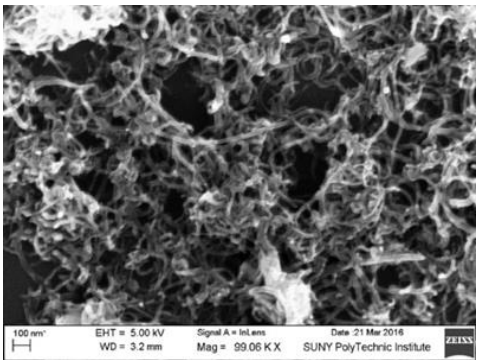

Figure 1: Bright and dim MWCNTs are circled in the image on the right to highlight where the EDS data was collected from

To verify that the copper is nucleated inside the tubes, TEM images were collected and they show partial filling of carbon nanotubes with copper. Unlike SEM, in TEM high atomic number materials such as Cu show as dark due to absorption of the electron beam, while the areas that transmit more electrons correspond to lighter atoms (such as carbon). TEM images in Figure 2 show success in partially filling the MWCNTs with Cu using $Cu(NO_3)_2$ solution.

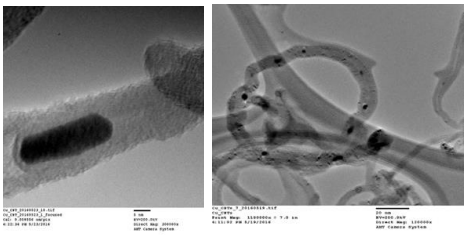

Figure 2: TEM images show that the carbon nanotubes are partially filled with copper.

3.2 Compositional analysis

To verify the copper filling of MWCNTs, EDS spectra were collected from the bright spots in the SEM images and compared to EDS data collected from dimmer areas in the MWCNT SEM images and to the Si background with no MWCNTs. The spectrum in figure 3, below, represent the composition of the sample imaged in figure 2.

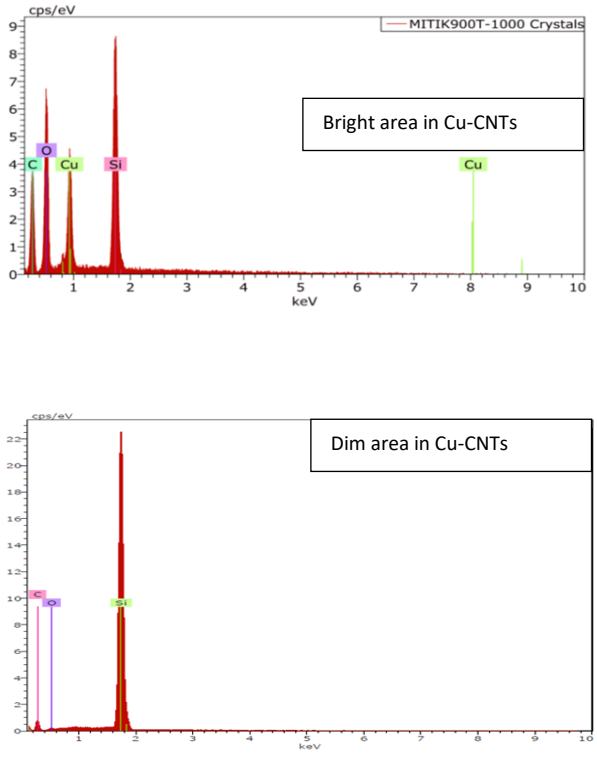

Figure 3: EDS spectra of two different areas in a sample prepared using Cu(NO3)2 solution.

The results show higher Cu content in the bright MWCNTs, from SEM imaging, compared to that from the less bright samples and from the background. However, due to the nature of this analysis technique, most of EDS signals are collected from more than 20 nm deep below the sample surface.

Therefore, the highest signal from each samples is always of Si. The carbon signal is a combination of signal of carbon nanotubes and contamination on the Si surface. The oxygen signal is from the surface contamination and functionalization of MWCNTs. The functionalization takes place in the opening process, during the acid reflux.

The same sample was analyzed by XPS, for surface characterization of the top few nanometers of the sample[10]. Because of that, the background silicon content is shown to be much lower in XPS than in EDS. In XPS, the initial scan is a survey to determine what elements exist in the sample. Following that, a high-resolution scan of each photoelectron peak is performed and this data is used for quantitative analysis of peak area and binding energy (Fig. 4).

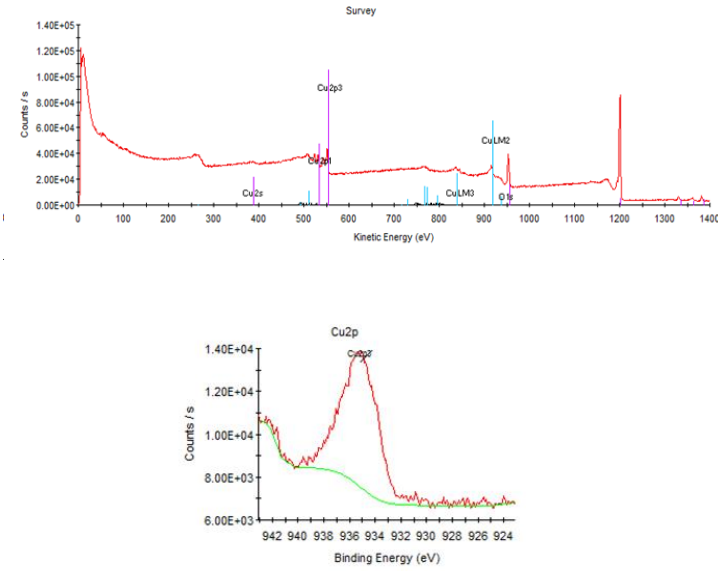

Figure 4: XPS spectra of analyzed data. The top spectrum is a survey of the sample while the bottom spectrum is a high-resolution scan of a copper peak

To study the effect of variation of the filling process, the reflux time and the molar concentration of the acid have been altered. Table 1 is a summary of the various reflux times and $Cu(NO3)_2$ salt concentrations used and the effects on measured copper concentration. Doubling the reflux time and the copper salt molar concentration increased the copper content by more than four and two-fold respectively.

Table 1: effect of doubling the acid reflux time and/or the copper salt molar concentration in copper filling

Set #	*Set 1*	*Set 2*	*Set 3*
HNO_3 reflux time	12 hours	24 hours	24 hours
$Cu(NO_3)_2$ molarity	0.87 mol/L	0.87 mol /L	1.74 mol/L
XPS Cu%	0.14 %	0.91%	1.71%
EDS Cu%	1.46%	4.43%	8.58%

4. DISCUSSION

In this study, we filled MWCNT's with copper using copper (II) nitrate under acid reflux. The collected data suggests that the filling procedure could be further optimized and is an element of further study. These data were consistent with both XPS and EDS, but both methods have drawbacks that need to be noted.

EDS is a very focused measurement, probing an area of a few nanometers in diameter and tens of nanometers depth. These measurements are focused on dim or bright regions and represent a small area, as such, they may not be representative of the whole sample. XPS complements this measurement in that these scans were over a region with diameter of 100 microns and depth to around 2-10 nm. The fact that these methods both lead to similar results, showing Cu existence in the studied sample and showing variation in the amount of copper with the alteration of the filling process, yields confidence that the data are consistent. However, quantitative conclusions based upon them are more difficult to draw as it can't be ruled out that some residue or surface copper was part of either measurement. This question should be part of further study in optimizing the filling procedure of MWCNT.

We used TEM to confirm that the copper in these MWCNT was, indeed, inside the nanotubes and not simply bound to the outside. Our TEM images show that we were successful in filling these nanotubes, but don't shed any light on whether there was surface copper or residue and to what degree. While we can say definitively that the MWCNT were partially filled with copper, measuring the amount and optimizing that process remains a subject of further study.

In the initial phase of this study, we used copper (II) nitrate to fill the nanotubes because this was a convenient and commercially available copper salt. The point, however, of this study is to demonstrate the feasibility of filling nanotubes

with 67Cu, which is typically available as a chloride salt. We repeated the experiment with copper (II) chloride and achieved similar results with similar concentrations and reflux times. (You should add a leading sentence explaining that the radioactive source would limit the metal ion concentration in the solution. The use of copper (II) chloride in concentrations equal to that which would be attainable with 67Cu, however, resulted in a very dilute solution which could not be measured with and of the methods we used here. However, the MWCNTs filled with non-radioactive Cu can be repurposed.

5. CONCLUSION

Partial filling of MWCNTs with Cu was observed under various processing conditions and using two types of copper solutions. These results show that it is feasible to fill carbon nanotubes with a radioactive Cu source for potential targeted radiotherapeutics applications. A variation of the Cu concentration was observed in the XPS and EDS data as a result of the variation of exposure time and concentration. However, TEM couldn't be used for quantification of the amount of copper in the MWCNTs, resulting in lack of confirmation of whether the increase in Cu is due to additional MWCNT filling rather than being due to residues around the MWCNTs. Replacing the $Cu(NO_3)_2$ with a $CuCl_2$ salt has also resulted in copper filled carbon nanotubes. This is a proof of concept of the feasibility of filling carbon nanotubes with Cu^{67}.

6. REFERENCES

[1] P. McEuen et.al., A. (2002). Single-Walled Carbon Nanotubes Electronics. IEEE Transactions on Nanotechnology, 1 (1), 78 – 85

[2] S. Ji et.al., A. (2010). Carbon Nanotubes in Cancer Diagnosis and Therapy. Biochimia et Biophysics Acta, 29 – 35.

[3] L. Williams et.al., A. (2008). Targeted Radionuclide Therapy. Medical Physics, 35 (7), 3062 – 3068.

[4] A. Ruggiero et.al., A. (2010). Imaging and Treating Tumor Vasculature with Targeted Radiolabeled Carbon Nanotubes. International Journal of Nanomedicine, 783 – 802.

[5] D. Peer et.al., A. (2007). Nanocarriers as an Emerging Platform for Cancer Therapy. Nature Nanotechnology, 2, 751 – 760.

[6] S. Hong et.al., A (2010). Filled and Glycosylated Carbon Nanotubes for in Vivo Radioemitter Localization and Imaging. Nature Materials, 9, 485 – 490.

[7] S. Murugesan et.al., A (2011). Amino-Functionalized and Acid Treated Multi-Walled Carbon Nanotubes as Supports for Electrochemical Oxidation of Formic Acid. Applied Catalysis B: Environmental, 103, 266 – 274.

[8] D. Ugarte et.al., A. (1998). Filling Carbon Nanotubes. Appl. Phys. A., 67, 101 – 105.

[9] N.I. Ayzatskiy, A. (2007). Comparison Of Cu-67 Production At Cyclotron andElectron Accelerator. Cyclotron and Their Applications, 243-245