UNIVERSITI PUTRA MALAYSIA

SYNTHESIS AND CHARACTERIZATION OF POLYHYDROXYETHYL-ACRYLATE AND POLYHYDROXYETHYLMETHACRYLATE GEL DOSIMETERS

KHALID AHMED MAJALI RABA'EH

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By

KHALID AHMED MAJALI RABA'EH

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

October 2007

In the Name of Allâh, the Most Gracious, the Most Merciful

ان الله يمسك السماوات والارض ان تزولا ولئن زالتا ان امسكهما من احد من بعده انه كان حليما غفورا

Surely Allah upholds the heavens and the earth lest they come to naught; and if they should come to naught, there is none who can uphold them after Him; surely He is the Forbearing, the Forgiving.

Al-Quran, 35:41

DEDICATION

To the Memory of my Lovely Son

Malik

Abstract of the thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of requirement for the degree of Doctor of Philosophy

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October 2007

Chairman: **Professor Elias Saion, PhD**

Faculty: **Science**

Polymer gel dosimeters in conjunction with the nuclear magnetic resonance imaging (MRI) are potentially used for verification of complex dose distributions in three dimensions (3*D*) for radiotherapy treatment planning. The radiation-induced polymerization of hydroxyethylacrylate (HEA) and hydroxyethylmethacrylate (HEMA) polymer gel dosimeters has been studied using Raman spectroscopy, nuclear magnetic resonance (NMR) and MRI scanner. The HEA polymer gels were synthesized from 2-hydroxyethylacrylate (HEA) monomer (2 to 5% w/w), *N*,*N*'-methylene-bis-acrylamide (BIS) cross-linker (2 to 5% w/w), gelatin (3 and 5%) and de-ionized water in oxygen free environment. The HEMA polymer gels were synthesized from 2-hydroxyethylmethacrylate (HEMA) monomer (2 to 5% w/w), BIS (2 to 5% w/w), 5% gelatin and de-ionized water. The dosimeters were irradiated with ^{60}Co teletherapy γ-ray source at a constant dose rate of 0.43 Gy/min, receiving

doses up to 20 Gy for a single point dose measurement and up to 30 Gy for 3*D* dose distributions scanning.

Raman spectroscopy was used to investigate directly the degree of radiation-induced polymerization and the rate of elapsed polymerization, targeting the COO stretching Raman shift at vibrational band of 1415 cm^{-1} assigned for HEA polymer gels and the OH stretching Raman shift at vibrational band of 3358 cm^{-1} assigned for HEMA polymer gels. The Raman intensity y corresponding to the amount of polymerization in both HEA and HEMA polymer gels increases with absorbed dose D in the dose range between 0 and 20 Gy and follows mono-exponential equation given as $y = y_0 + A(1 - e^{-D/D_0})$. The rate of elapsed polymerization in HEA and HEMA polymer gels decreases with absorbed dose in the dose range between 0 and 20 Gy and follows exponential equation given as $\frac{dy}{dt} = \frac{A\kappa}{D_0} e^{-D/D_0}$. The dose sensitivity, D_0 of polymerization and the half dose, $D_{1/2}$ of the rate of elapsed polymerization in HEA and HEMA polymer gels increase strongly with increasing the cross-linker concentration than that of the monomer concentration where the dose correlation factor for the cross-linker is always greater than the dose correlation factor for the monomer. At 3% gelatin the D_0 and $D_{1/2}$ values of the HEA polymer gels always greater than at 5% gelatin, indicating that the polymerization and the rate of elapsed polymerization of HEA polymer gels increases with decreasing the amount of gelatin. The consumption of co-monomer in HEA and HEMA polymer gels decreases mono-exponentially with absorbed dose in the dose ranges between 0 and 20 Gy and it follows mono-exponential equation of the form $y = y_0 - A\left(1 - e^{-D/D_0}\right)$.

The result shows that the cross-linker consumption increases more significantly with absorbed dose than the monomer consumption.

The nuclear magnetic resonance (NMR) spin–spin relaxation rate, R_2 for water proton surrounding the polymer formation has been used to investigate indirectly the degree of polymerization and the rate of elapsed polymerization of HEA and HEMA polymer gels. The dose response of the change in relaxation rate, ΔR_2 is also mono-exponential function and for the rate of elapsed polymerization it is normal exponential function. The dose sensitivity, D_0 for the change in relaxation rate ΔR_2 and the half dose, $D_{1/2}$ for the rate of elapsed polymerization of HEA and HEMA polymer gels have produced results of similar trend to that of Raman spectroscopy method.

The radiological film obtained from the clinical MRI scans of polymer gel phantom to simulate radiotherapy treatment planning was analyzed using a densitometer. The optical density of the polymer gels was found to increase with the increase of absorbed dose and decreases with the increase of depth inside the phantom. The dose-depth map for HEA polymer gels was derived for different concentrations of HEA and BIS co-monomers. The results suggest that for a clinical radiotherapy treatment planning the dose correction for tumour deep within the body should be implemented with knowledge of the amount of applied dose, tumour volume, skin to tumour distance, and tissue equivalent nature of the body. The percentage of depth dose was also evaluated which leads to a good agreement with the ionization chamber measurements.

The indirect measurements of HEA and HEMA polymer gels using NMR have shown more dose sensitivity than that for direct measurements using Raman spectroscopy. In general the dose sensitivity and half dose of HEA polymer gels are grater than that for HEMA, indicating that the HEA polymer gels are more radiosensitive than that of HEMA polymer gels at a given dose. The dose-depth map has been achieved using HEA polymer gels in conjunction with MRI scanning which led to introduce a fit equation between dose and depth inside HEA polymer gels.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

SINTESIS DAN PENCIRIAN POLIHYDROXYETHYLACRYLATE DAN POLIHYDROXYETHYLMETHACRYLATE DOSIMETER GEL

By

KHALID AHMED MAJALI RABA'EH

Oktober 2007

Pengerusi: **Profesor Elias Saion, PhD**

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Dosimeter polimer gel dan imej resonan magnet nuclear (MRI) mampu digunakan untuk menentusahkan taburan dos komplek tiga dimensi (3*D*) untuk kegunaan pelan rawatan radioterapi. Pempolimaran induksi sinaran bagi dosimeter polymer gel hydroxyethylacrylate (HEA) and hydroxyethylmethacrylate (HEMA) telah dikaji dengan menggunakan Raman spectroskopi, resonan magnet nuklear (NMR) dan imbas MRI. Polymer gel HEA disentisis menggunakan monomer 2-hydroxyethylacrylate (HEA) (2% hingga 5% w/w), petautsilang *N*,*N*'-methylene-bis-acrylamide (BIS) (2% hingga 5% w/w), gelatin (3% dan 5%) dan air tak berion dalam keadaan bebas oksigen. Manakala polimer gel HEMA disentisis dengan menggunakan monomer 2-hydroxyethylmethacrylate (HEMA) (2 hingga 5% w/w), BIS (2% hingga 5% w/w), 5% gelatin dan air tak berion. Semua dosimeter didedahkan kepada sinar gama daripada sumber ^{60}Co teletherapy pada kadar dos 0.43

Gy/min dan menerima dos hingga kepada 20 Gy bagi pengukuran dos titik tunggal dan hingga kepada 30 Gy bagi pengukuran imbasan taburan dos 3*D*.

Darjah pempolimeran induksi sinaran dan kadar pempolimeran lepasan telah dikaji secara terus menggunakan spectroskopi Raman dengan mensasarkan kepada anjakan Raman rengangan COO pada jalur getaran 1415 cm^{-1} yang ditujukan kepada polimer gel HEA dan anjakan Raman rengangan OH pada jalur getaran 3358 cm^{-1} yang ditujukan kepada polimer gel HEMA. Keamatan Raman y sepadan dengan amaun polimeran bagi kedua HEA and HEMA bertambah dengan dos terserap D dalam julat dos di antara 0 dan 20 Gy dan memenuhi persamaan mono-eksponen dinyatakan sebagai $y = y_0 + A(1 - e^{-D/D_0})$. Kadar polimeran lepasan HEA dan HEMA berkurang dengan dos terserap dalam julat dos di antara 0 dan 20 Gy dan memenuhi persamaan eksponen diberi sebagai $\frac{dy}{dt} = \frac{A\kappa}{D_0} e^{-D/D_0}$. Kepekaan dos, D_0 untuk proses polimeran dan dos separuh, $D_{1/2}$ untuk kadar polimeran lepasan bagi gel HEA and HEMA bertambah dengan banyaknya dengan pertambahan kepekatan petautsilang melebihi yang diperolehi daripada kepekatan monomer dimana factor korelasi dos petautsilang lebih tinggi daripada factor korelasi dos monomer. Nilai D_0 dan $D_{1/2}$ adalah lebih tinggi bagi polimer gel HEA dengan 3% gelatin berbanding dengan 5% gelatin, menunjukkan pempolimeran dan kadar pempolimeran lepasan polymer gel HEA bertambah dengan pengurangan kepekatan gelatin. Penggunaan ko-monomer dalam polymer gel HEA and HEMA berkurangan secara mono-eksponen dengan dos terserap dalam julat dos di antara 0 dan 20 Gy dan memenuhi persamaan absorbed dose in the dose ranges between dalam bentuk $y = y_0 - A\left(1 - e^{-D/D_0}\right)$. Keputusan

menunjukkan bahawa penggunaan petautsilang adalah lebih tinggi berbanding penggunaan monomer.

Kadar santaian spin-spin resonans magnet nuclear, R_2 untuk air di sekeliling pembentukan polimer telah digunakan untuk menyelidiki secara tak terus menggunakan darjah pempolimeran dan kadar pempolimeran lepasan bagi polimer gel HEA and HEMA. Sambutan dos terhadap perubahan kadar santaian, ΔR_2 adalah juga fungsi mono-eksponen dan kadar pempolimeran lepasan adalah juga fungsi eksponen. Keputusan mengenai kepekan dos, D_0 untuk perubahan kadar santaian ΔR_2 dan dos separoh, $D_{1/2}$ untuk kadar pempolimeran lepasan polimer gel HEA dan HEMA mempunyai haluan yang sama dengan kaedah spektroskopi Raman.

Sebuah pengimbas kilinik MRI telah digunakan bagi mendapatkan film radiology fentom polimer gel untuk simulasi plan rawatan radioterapi yang dianalisis dengan menggunakan sebuah densitometer. Ketumpatan optik polimer gel didapati bertambah dengan dos terserap dan berkurangan dengan pertambahan kedalaman fentom. Peta hubungan dos-kedalaman bagi polimer gel HEA telah dihasilkan untuk kepekatan ko-monomer HEA dan BIS yang berbeza. Keputusan menunjukkan bahawa untuk plan rawatan radiotrepi pembetulan dos tumour dalam badan perlu dilakukan dengan mengetahui amaun dos dikenakan, isipadu tumour, jarak diantara kulit dan tumour dan kesetaraan tisu badan. Peratus dos kedalaman telah ditentusahkan dan didapati bersetuju dengan pengukuran dengan menggunakan kebok pengion.

Pengukuran secara tak langsung gel polimer HEA dan HEMA menggunakan NMR telah menunjukkan dos kepekaan yang lebih berbanding pengukuran secara langsung menggunakan spektroskopi Raman. Secara amnya, dos kepekaan dan dos separa untuk gel polimer HEA adalah lebih tinggi daripada HEMA, menunjukkan bahawa gel polimer HEA lebih radiosensitif berbanding gel polimer HEMA pada dos yang tertentu. Peta kedalaman dos telah diperolehi dengan mengunakan gel polimer HEA bersama dengan imbasan MRI yang menjurus kepada pengenalan persamaan padanan di antara dose dan kedalaman di dalam gel polimer HEA.

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I should thank my mother for my upbringing and for the support of my receiving high education and also I would like to thank my wife and my son Mohammad for their patience, encouragement and understanding

I certify that an Examination Committee met on 3rd October to conduct the final examination of Khalid Ahmed Majali Raba'eh on his Doctor of Philosophy thesis entitled "Synthesis and Characterization of Polyhydroxyethylacrylate and Polyhydroxyethylmethacrylate Gel Dosimeters" in accordance with Universiti Pertanian Malaysia (Higher Degree) Act 1980 and Universiti Pertanian Malaysia (Higher Degree) Regulations 1981. The Committee recommends that the student be awarded the degree of Doctor of Philosophy.

Members of the Examination Committee were as follows:

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Date: 22 November 2007

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfillment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

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Date: 13 December 2007

DECLARATION

I declare that the thesis is my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at universiti Putra Malaysia or at any other institution.

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KHALID AHMED MAJALI RABA'EH

Date: 2007

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