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Effects of Ho: YAG Laser (2100nm) in Prostate Tissue: An in vitro Study

Ali S. Mahmood (1) **Omar S. Khattab** (2) **Saba Y. Tanno** (3)

(1,3) Institute of Laser for Postgraduate Studies, University of Baghdad, Baghdad, Iraq
(2) College of Medicine, University of Baghdad, Baghdad, Iraq

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Abstract: Background: Benign prostate hyperplasia (BPH), non-cancerous enlargement of prostate, is the most prevalent disease entity in elderly men. BPH affects 40% of men after the age of 60year worldwide. BPH causes problems for patients with significant lower urinary tract obstructive symptoms, if not responding to medical therapy, surgical intervention is instituted. One method of the treatment of symptomatic BPH is laser prostatectomy. The understanding of tissue effects by laser radiation is very important for the safe clinical application of laser. **Objective**: study the 2100 nm Ho: YAG laser gross tissue effects in the prostate at different laser dose settings in an vitro model prostate tissue samples harvested from same specimen of open surgery prostatectomy. **Materials and methods**: Specimen of same open surgery prostatectomy was sectioned into six samples preserved in 4% formalin solution. Laser irradiations were performed in ambient air at room temperature. Samples exposed to varying laser dose parameters using pulsed Ho: YAG laser. The laser settings consisted of energy per pulse (0.3, 0.5 and 1 J), and pulse repetition rate (10 and 25 Hz) in single or double pulse mode. Pulse duration was 350 µs. Laser radiation was delivered using laser fibers with an optical core diameter of 550 µm. Main evaluation criteria of the Ho::YAG laser performance in prostate tissue was made by visual gross appearance of the effects of incision, cutting, vaporization, ablation and coagulation properties. **Results:** high laser dose setting revealed ablation, vaporization, incision, and cutting performance. Also there was clear evidence of coagulation zone. There was no clear appearance of carbonization. Sometimes minimum carbonization effect noticed. Ablation of prostate tissue was achieved by low dose setting. High and Low settings were responsible for coagulation effect. **Conclusion:** different dose parameters including energy per pulse, pulse repetition rate and in single or double pulse mode provide an effective way for ablation, vaporization, incision, cutting and coagulation effects in the prostate tissue.

Key words: Benign prostatic hyperplasia, Laser therapy, Vaporization, Coagulation, Incision, Prostatectomy and Ho: YAG laser.

Introduction

Patients with symptomatic BPH are initially treated by medical therapy (namely α-adrenergic blockers), and when treatment failed they are advised to undergo surgery. Prostate removal can be performed in a number of different ways depending on symptoms and size of the prostate (Gilling PJ et. al 2012).The three most common procedures for removing non-cancerous enlargement of the prostate are:

1. Transurethal resection of the prostate (TURP)
2. Open prostatectomy.
3. Laser prostatectomy.

Transurethral resection of the prostate (TURP), an endoscopic procedure where prostate tissue is sequentially removed with an electrocautery loop, remains the gold standard to which other surgical therapies are compared. Unfortunately, TURP is associated with significant patient morbidity such as blood loss and dilutional hyponatremia, especially when resection times are prolonged (Mottet N, et al 1999).Because of the long resection times and increased morbidity risks involved in patients with extremely large prostate glands, open simple prostatectomy was traditionally employed in place of TURP to remove the obstructing adenoma tissue. However, the patient could still expect a prolonged hospital stay and a high likelihood of post-operative complications (Kabalin JN, 1996). Over the past few years, several laser devices were introduced in urologic surgery. The pulsed Ho:YAG laser, with a wavelength of 2100 nm, is the most commonly used laser because of its wide field of applications regarding tissue surgery and stone treatment. This energy source has become the standard tool for intracorporal lithotripsy in percutaneous or retrograde intrarenal surgery (Gupta 2007; Pierre and Preminger 2007). The Ho: YAG laser radiation is highly absorbed in any water containing material, such as tissue or urinary stones, leading to an instant vaporization and a low penetration depth (Herrmann et al. 2012; Teichmann et al. 2007). One advantage of Holmium laser enucleation of prostate (HoLNP) over TURP is that the procedure is suitable for large prostates. Outcomes after treatment may rival those of open prostatectomy, the gold standard treatment for BPH in large prostates. HoLEP has been compared in several studies to open prostatectomy. Naspro et al. evaluated 80 patients randomized to HoLEP or open prostatectomy for 2 years following treatment (Naspro et al. 2006). Hospital stay, blood loss, and blood transfusion rate were lower in the HoLEP group but operative time was shorter in the open prostatectomy group. Improvements in urodynamic and uroflowmetry were similar at 24 months. Kuntz et al. randomized 120 patients with prostates greater than 100 g to either HoLEP or open prostatectomy (Kuntz et al. 2008). At 5 years, improvements in micturition were equivalent and reoperation rates were similarly low. Elzayat et al. published a series of 225 patients with prostate size greater than 80 g who underwent HoLEP. The authors found the procedure to be safe and effective (Elzayat and Elhilali 2006).The HoLEP is safe and effective procedure for treatment of BPH with durable outcomes. The procedure is safer and just effective as effectness as TURP and open prostatectomy in patients on anticoagulation and in those with large prostates. Unfortunately the HoLEP is limited by high learning curve and the need for using a morsellator. (Elzayat and Elhilali 2006).

Materials and Methods:

This study was conducted at the laser medicine research clinic of the institute of laser for postgraduate studies, University of Baghdad, as part of the pioneer project **"Laser Prostatectomy**”. This work was done from September 2010 to February 2011.

Materials:

Samples of prostate tissue:

Specimen of prostate tissue harvested from same open surgery prostatectomy was sectioned into six samples; three samples were 8 mm in thickness, three samples were 15 mm in thickness; all samples were preserved in 4%formalin.

Laser system:

The Specifications of **Omni Pulse MAX^{TM} 80 Watt Holmium laser system Model 1210** used in this work are: Ho: YAG laser operates in pulse regimen with transmission of radiation along the fiber 550 µm in diameter (maximum output power 80 W, single pulse mode with repetition rate 5 - 60 Hz and double pulse mode with repetition rate 3-30 Hz, energy rate per one pulse 0.2 - 3.5 J, and 350 µs pulse duration). In Double pulse mode, according to manufacturer, twin pulses are spaced to allow the effects of the first pulse to subside before the second pulse arrives. The Ho: YAG laser emits laser radiation at a wavelength of 2100 nm in a pulsed manner. The output of the Ho: YAG laser is set separately for pulse energy in joule (J) and pulse repetition rate in Hertz (Hz).

Methods and Laser irradiation parameters:

Each sample, preserved in 4%formalin, was washed with normal saline (0.9% sodium chloride) solution prior to laser irradiation.

Procedures were done in ambient air at room temperature. Laser delivery to the tissue was carried out in a standardized setup. The tissue surface of each sample was exposed to laser irradiation under visual guidance. During the irradiation procedures specific eye protective goggle was worn. The angle between the fibers to the tissue surface was approximately 90°. Experiments were performed with approximately speed of 2 mm/s. The distance between the fiber tip and the tissue was in contact technique and sometimes about 0.5 mm. Pulse duration was 350 µs. For delivery of laser radiation a laser fiber with an optical core diameter of 550 µm was used. The fiber was cut prior to every single experiment by special fiber cutter. Exposure time in each sample was measured using stopwatch.

Laser irradiation parameters: Table 1 display the laser irradiation parameters used in this experimental work in the six prostate samples (three samples were 8 mm in thickness, and further three samples were 15 mm in thickness) harvested from the same open surgery prostatectomy specimen.

Table 1: Laser Irradiation Parameters.

Sample No.	Thickness of Sample= mm	Energy per Pulse =Joule	Pulse Repetition Rate =Hz	Pulse Mode Single /Double
1	**8**	**0.5**	**20**	**double**
2	**8**	**1**	**10**	**double**
3	**15**	**1**	**10**	**double**
4	**8**	**1**	**10**	**single**
5	**15**	**1**	**10**	**single**
6	**15**	**0.3**	**25**	**double**

Sample No. 1 (the thickness of this sample = 8 mm), exposed to the following laser dose parameters: energy per pulse was 0.5 J; pulse repetition rate was 20 Hz, in double pulse mode. Exposure time was 108 sec.

On Sample No. 2 (the thickness of this sample = 8 mm) the following parameters were used including energy per pulse= 1 J, pulse repletion rate equals 10 Hz, and in double pulse mode. Exposure time was 180 sec.

On sample No. 3 (sample thickness = 15 mm) the following parameters were used energy per pulse 1 J, pulse repetition rate 10 Hz, in double pulse mode. Exposure time was 180 sec.

While on the **sample No. 4** (the thickness of this sample = 8 mm), laser dose parameters used were energy per pulse 1 J, pulse repetition rate 10 Hz, in single pulse mode. Exposure time was 30 sec.

For **sample No. 5 (**sample thickness = 15 mm) the following laser dose parameters were used: energy per pulse 1 J, pulse repetition rate 10 Hz, in single pulse mode. Exposure time was 60 sec.

On Sample No. 6 (sample thickness = 15 mm) the following parameters were used: energy per pulse was 0.3 J, pulse repetition rate 25 Hz, in double pulse mode. Exposure time was 30 sec.

At the end of each experimental work, vaporization, incision, cutting, ablation and coagulation effects of the 2100 nm Ho: YAG laser performance were described by visual gross appearance as main evaluation criteria.

Energy density was calculated as applied energy divided by area (area was 0.0024 cm^2). So dose estimated as energy density times pulse repetition rate. Total dose energy delivered inside the treated tissue calculated by multiplication the estimated dose times the exposure time.

Results: In this an in vitro works, the effects of varying dose parameters (pulse energy, pulse repetition rate, pulse mode) of Ho: YAG laser in prostate tissue were described by gross visual appearance as main evaluation criteria. Different energies, pulse repetition rates and in single or double pulse mode were used in six prostate samples from same open surgery prostatectomy specimen.

As shown in **Figure 1** for sample no. 1, when the energy density was 208 J/cm^2. Estimated Dose was 4160 J. Total energy deposited inside the treated area was 449280 J during 108 sec exposure time .There was evident appearance of ablation, vaporization and incision effects without coagulation or carbonization.

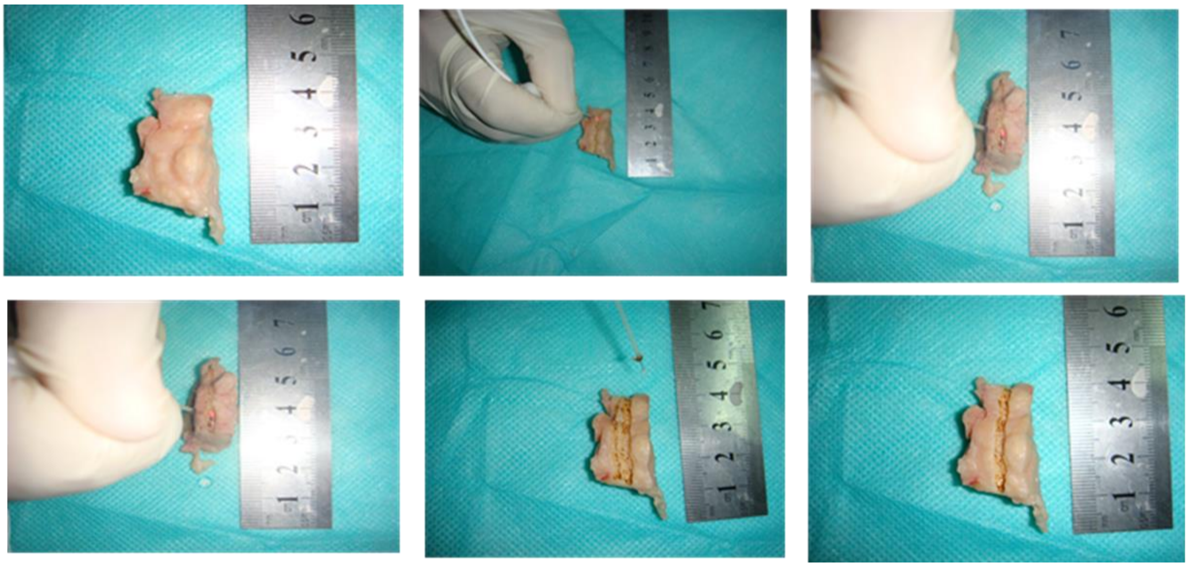

Fig. 1: Sample No.1: Energy per pulse (EP) = 0.5 J, Pulse Repetition Rate (PRR) =20 Hz, and in double pulse mode.

As shown in **Figure 2** for sample no. 2, when the energy density was 417 J/cm^2. Estimated Dose was 4167 J. Exposure time was 180 sec. Total energy dose was 750600 J delivered during exposure time. There was clear evidence of vaporization and cutting with coagulation effects.

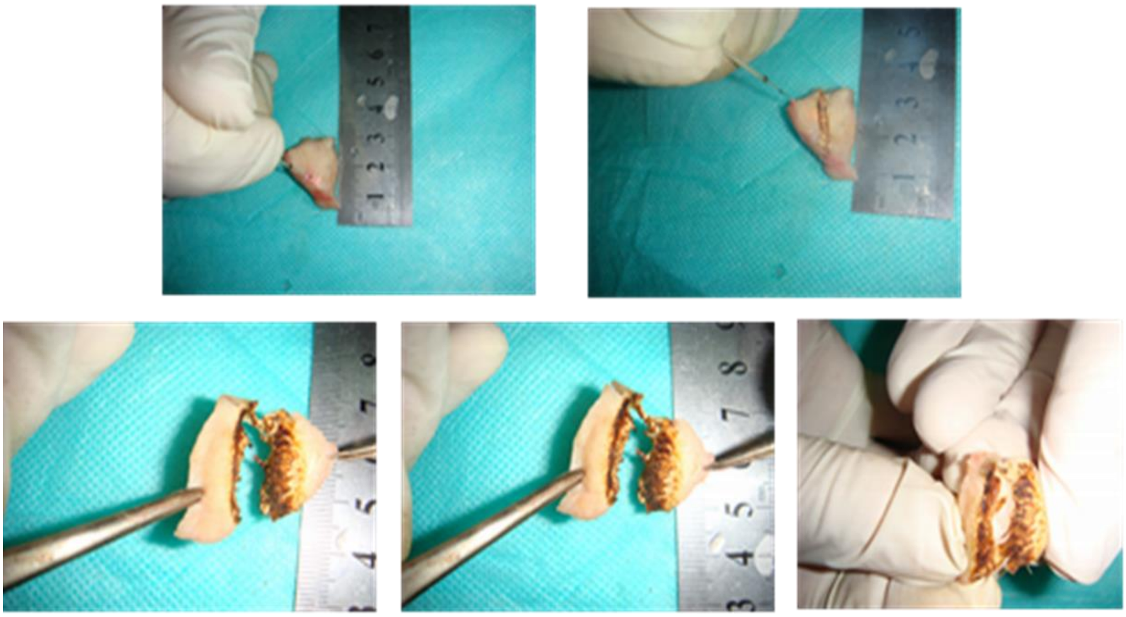

Fig. 2: Sample No.2 E/P = 1 J, PRR = 10 Hz and in double mode

As shown in **Figure 3** for sample no. 3, when ED was 417 J/cm^2 Estimated Dose was 4170 J. Exposure time was 180 sec. The deposited total energy was 750600 J during the exposure time. There was an efficient ability to cut the prostate tissue with coagulation zone at the margins.

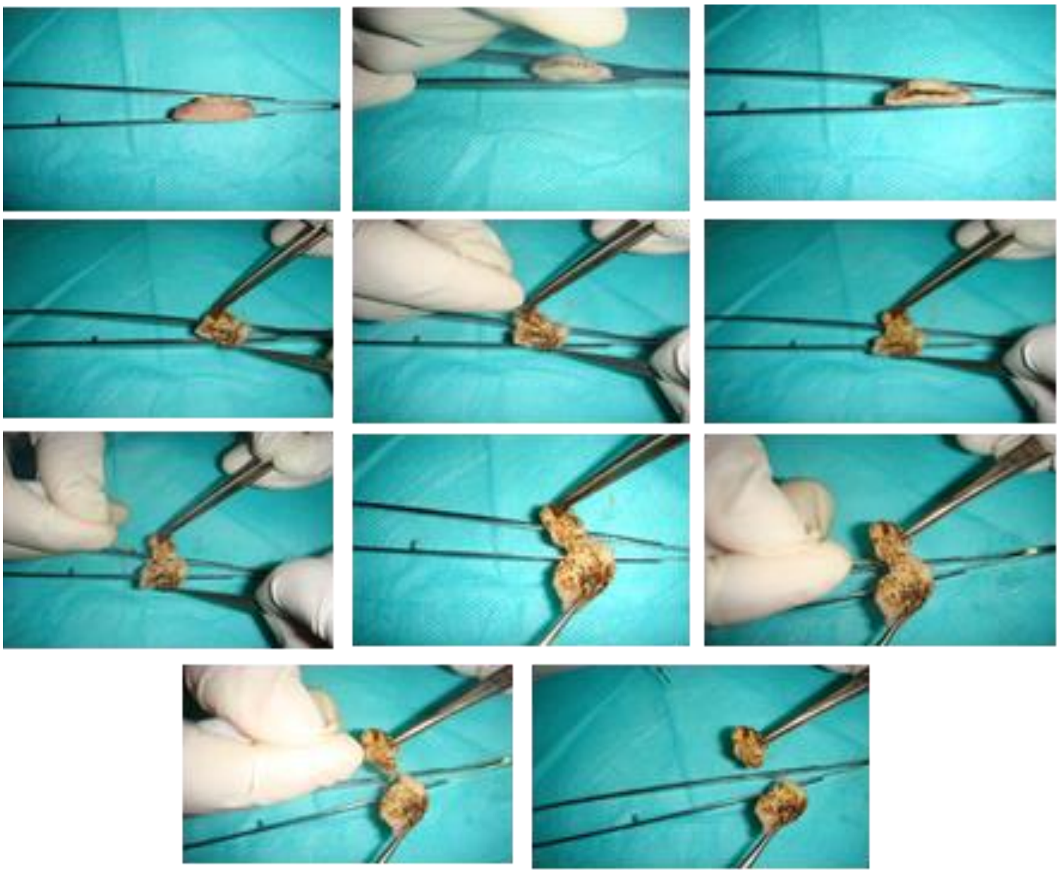

Fig. 3: Sample No.3 EP= 1 J, PRR = 10 Hz, and in double pulse mode.

As shown in **Figure 4** for sample no. 4, when the ED was 417 J/cm ^{2}. Estimated Dose was 4170. While total energy was 125100 J during 30 sec exposure time. There was clear evidence of ablation with minimal coagulation.

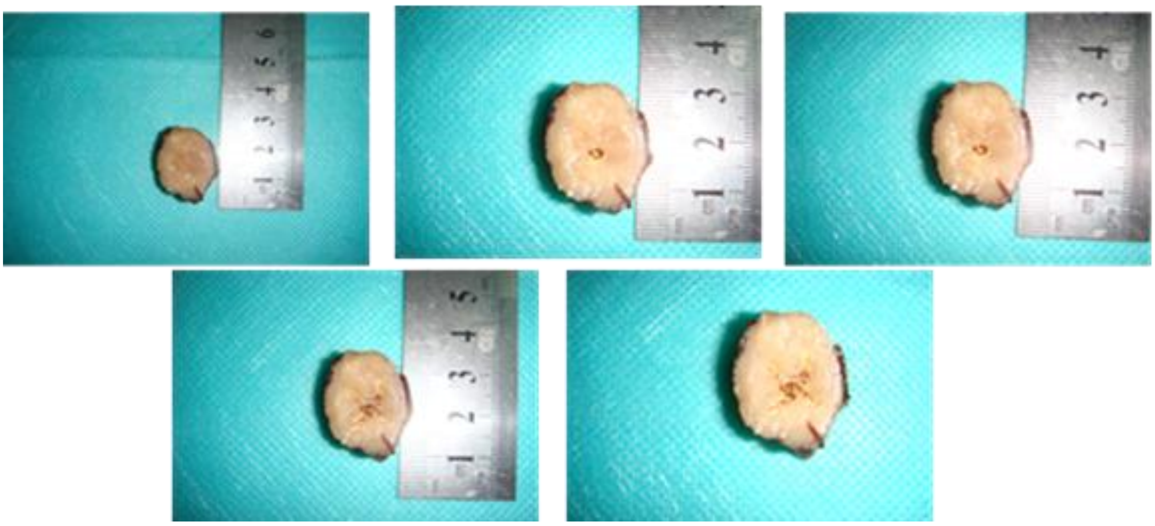

Fig. 4: Sample No. EP = 1 J, PRR = 10 Hz, and in single pulse mode.

As shown **Figure 5** for sample no. 5, when the ED= was417J/cm ^{2}. Estimated Dose was 4170J. Exposure time was 60sec. While total energy was 250200J. There was clear evidence of vaporization and incision effects.

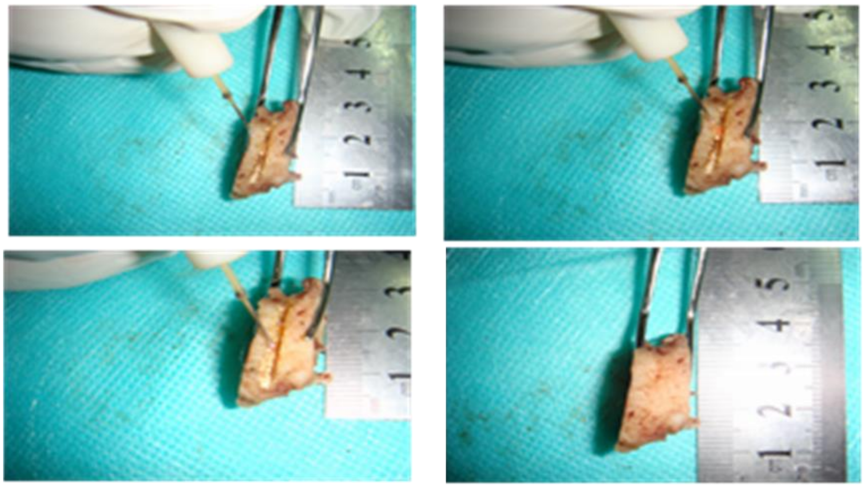

Fig. 5: Sample No.5 EP= 1J, PRR= 10 Hz, and in single pulse mode.

As shown in **Figure 6** for sample no. 6, when the ED was 125 J/ cm ^{2},). Estimated Dose was 3125 J. Exposure time was 30 sec. The total energy was 93150 J. There was evidence of ablation with minimum coagulation effects.

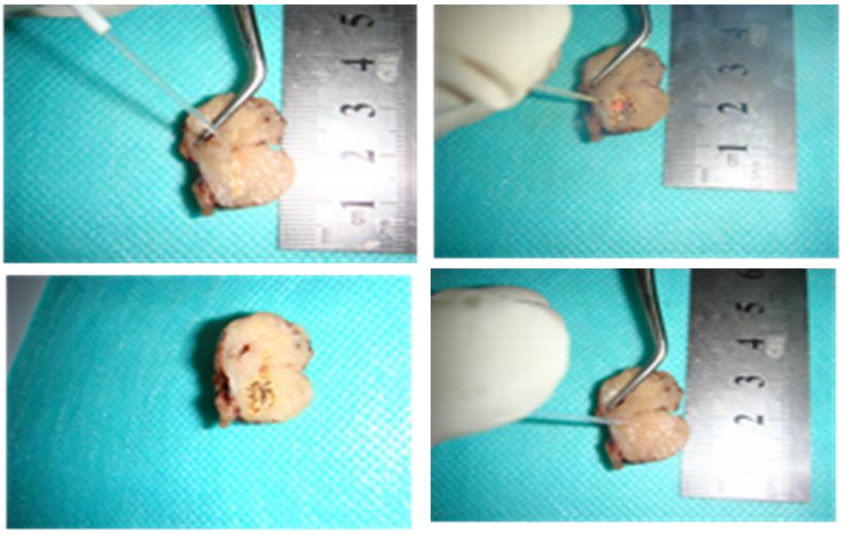

Fig. 6: Sample No.6 EP = 0.3 J, PRR=25 Hz, and in double pulse mode.

Table 2 shows the different applied energy, area, estimated energy density, pulse repetition rate, exposure time, and deposited total energy during exposure time and effects.

High dose setting revealed vaporization, incision, cutting performance by pulsed Ho: YAG Laser. There was clear evidence of coagulation zone. Also there was no clear appearance of carbonization and sometimes there was a minimal carbonization effect. In laser vaporization, high delivered laser dose, energy and energy density was responsible for the tissue vaporization. Ablation of prostate tissue achieved by low dose setting. High and Low dose settings were responsible for laser coagulation effects due to photothermal interaction mechanism of laser.

Regarding pulse mode effect there was no clear evident difference between single and double pulse mode application but probably the effect may play an important role in the laser assisted urinary stone fragmentation.

Table 2: Different laser doses and its effects.

Sample No.	Energy -J	Area cm^2	E/D J/cm^2	PRR Hz	Estimated Dose –J-	Exposur-e time –Sec-	Total dose energy J	Gross visual effect
1	**0.5**	**0.0024**	**208**	**20**	**4160**	**108**	**449280**	Ablation, vaporization and incision without coagulation or carbonization.
2	**1**	**0.0024**	**417**	**10**	**4170**	**180**	**750600**	Clear vaporization and cutting with coagulation
3	**1**	**0.0024**	**417**	**10**	**4170**	**180**	**750600**	Cutting with coagulation zone at the margins.
4	**1**	**0.0024**	**417**	**10**	**4170**	**30**	**125100**	ablation with minimal coagulation
5	**1**	**0.0024**	**417**	**10**	**4170**	**60**	**250200**	vaporization and incision effects
6	**0.3**	**0.0024**	**125**	**25**	**3125**	**30**	**93750**	ablation with minimum coagulation effects

Discussion: Several lasers were introduced in urological surgery and stone treatment during the recent past decades. One of the most widely researched laser devices is the Ho: YAG laser. Holmium laser enucleation of prostate (HoLEP) has become a comparable treatment option to TUR in BPH therapy with advantages in the treatment of large prostatic adenomas (Herrmann et al. 2012; Gilling et al. 2000, 2012). In addition, the Tm: YAG laser was introduced and showed convincing results for treatment of BPH in several studies (Bach et al. 2010; Netsch et al. 2012). Based on the different physical properties of each laser system, additional ex vivo experiments are necessary to understand the effect on tissue and to assess the complications and the clinical outcome after surgery.

The holmium laser is a pulsed solid-state laser with a wavelength of 2100 nm. It is strongly absorbed by water. The absorption length in prostatic tissue is only 0.4 mm, and the resulting energy density is high enough to heat prostatic tissue to temperatures more than 100ºC, which creates vaporization without deep penetration and coagulation. This allows clean char-free and precise cutting, incision, and dissection of the prostatic lobes under endoscopic control when the laser fiber is brought into direct contact with and moved through the prostate. Dissipating heat causes simultaneous coagulation of small and medium-sized vessels, to a depth of 2–3 mm (Gilling PJ, et al, 1998 and Kabalin JN, et al, 1998). These unique properties of the holmium laser cannot only make it a useful tool for prostate surgery but also the ideal intracorporeal lithotripter for virtually all stones and an ideal wavelength for endoscopic multiple soft-tissue applications such as ablation of tumors and incision of strictures of the upper and lower urinary tract. Ho: YAG laser was used primarily for endoscopic interventions. Its use for open surgery is also promising. Further practical experience with Ho: YAG laser will provide additional information on its indications in urological diseases.

There are two basic principles of laser therapy for BPH. These are determined by the final tissue effect (what does the laser do to the tissue). These principles are laser coagulation and laser vaporization. The amount of energy delivered by the laser to the tissue determines the result of tissue coagulation or vaporization.

In laser coagulation, relatively low-density laser thermal energy is used to produce tissue coagulative necrosis, with a potential for delayed anatomical debulking. Clinically significant anatomical debulking occurs only if the tissue is allowed to slough, which takes place when the prostatic urothelium is involved in the process. Preservation and protection of the prostatic urothelium from laser thermal damage prevents tissue sloughing.

For laser vaporization, higher-density laser thermal energy is used. This high energy raises the tissue temperature to several hundred degrees Celsius, causing tissue vaporization. Additionally, various degrees of coagulation effects take place in the adjacent residual tissue. This principle is used in different ways to achieve a variety of objectives, depending on the amount and size of tissue vaporization. This range from complete tissue vaporization to incision, resection, or enucleation of the obstructing prostatic tissue. Irrespective of the technique used, the final common result is "opening" (i.e., anatomical deobstruction) of the prostatic urethra.

Conclusion

Based on the present findings, this study demonstrates that Ho: YAG lasers emitting laser radiation at 2.1 µm wavelength using different parameters laser setting including pulse repetition rates (10 and 25Hz) and energy per pulse (0.3, 0.5 and 1 J) in single or double pulse mode provide an effective way of vaporization, ablation, cutting, and coagulation of prostate tissue. The holmium: YAG (Ho: YAG) laser wavelength's ability to vaporize and incise soft tissue offers potential advantages for prostatectomy. This can be translated that Ho: YAG laser contributes and offers better cutting, incision, vaporization and coagulation, and BPH can be managed trans-urethrally after hands-on well trained program as well as high learning curve.

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أثار الهولميوم يا ك ليزر (2100نانومتر) في نسيج البروستات : دراسة خارج الجسم

علي شكر محمود(1) **عمر سالم خطاب**(2) **صبا يوسف تنو**(3)

(1،3) معهد الليزر للدراسات العليا ، جامعة بغداد، بغداد ، العراق
(2) كلية الطب ، جامعة بغداد، بغداد ، العراق

الخلاصة:- الخلفية: تضخم البروستات الحميد ,هو تضخم غير السرطاني للبروستات هو اكثر الامراض انتشارا بين الرجال المسنين. تضخم انسجة البروستات الحميدة يصيب 40% من الرجال بعد سن الستين سنة قي جميع انحاء العالم. تضخم انسجة البروستات الحميد يسبب للمرضى اعراض انسدادية للمجاري البولية السفلى والتي لا تستجيب للمعالجة الطبية يستوجب للتداخل الجراحي . واحدة من هذه الطرق هو استئصال البروستات بالليزر. فهم التاثير النسيجي لشعاع الليزر مهم جدا للتطبيق ألسريري الأمن لليزر . الهدف من الدراسة: دراسة تأثير الأنسجة الإجمالي لهولميوم يا ك ليزر (2100 نانومتر) في إعدادات جرعة ليزر مختلفة في عينات أنسجة بروستات . أجريت الدراسة في المختبربأستخدام الليزر على عينات من نموذج البروستات تم استئصالها من مريض أجريت له عملية جراحية مفتوحة لاستئصال البروستات. المواد والطرق: تم تقسيم نموذج من نفس جراحة البروستات المفتوحة إلى ست عينات حفظت في 4 ٪ محلول الفورمالين. أجريت عمليات التشعبع بالليزر في الهواء المحيط عند درجة حرارة الغرفة. عرضت العينات لمعلمات جرعة الليزر المختلفة باستخدام ليزر نابض. تتكون إعدادات الليزر من الطاقة لكل نبضة (0.3 ، 0.5 و 1 جول) ، ومعدل تردد النبض (10 و 25 هرتز) في وضع النبض المفرد أو المزدوج. كانت مدة النبضة 350 مايكرو ثانية. تم توصيل إشعاع الليزر باستخدام ألياف الليزر مع قطر الأساسية البصرية من 550 مايكرو متر. وتم تقيم التأثير الشقي و القطعي و التخثيري والتبخيري والجذ لأداء الليزر بواسطة المظهر الإجمالي المرئي للتأثير كمعايير التقييم الرئيسية . النتائج: ان جرعة ليزر عالية الطاقة كشفت عن الجذ و التبخير و، الشق ، وأداء القطع. كما كان هناك دليل واضح على منطقة تخثر. لم يكن هناك مظهر واضح للكربنة أو التفحم. في بعض الأحيان لوحظ الحد الأدنى لتأثير للكربنة. تم تحقيق جذ أنسجة البروستاتا عن طريق وضع إعداد جرعة منخفضة. كانت الإعدادات العالية والمنخفضة مسئولة عن تأثير التخثر. الاستنتاج: إن معلمات الجرعة المختلفة ، بما في ذلك الطاقة لكل نبضة ، ومعدل تكرار النبض ، وفي وضع النبض المفرد أو المزدوج ، توفر طريقة فعالة لتأثيرات التبخير ، والشق ، والقطع والتخثر في نسيج البروستات.