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Research Article

Dosimetric comparison between patients with a brain tumor by using three-dimensional conformal radiotherapy (3DCRT)

Fatihalla F Hassan [1*], Nashwan Karkhi Abdulkareem[1], Ilham Khalid Ibrahim[1], Dler Khalid Ismail[1].

[1]Department of Basic Science- Biophysics Unit, College of Medicine, Hawler Medical University (HMU), KR, Iraq.

Abstract

Background and objective: Three-dimensional conformal radiotherapy (3DCRT) is an advanced radiation treatment technique that shapes the radiation beams to match the shape of the tumor and it is used to treat brain tumors while avoiding radiation to the healthy tissue surrounding brain tumor. The purpose of this study is to evaluate the dosimetric data among the patients with a brain tumor by using three-dimensional conformal radiotherapy (3D-CRT).

Methods: In eight patients with brain tumors being treated by 3DCRT, the target, lenses of eyes, optic nerves, brain stem, and open chiasm were contoured. Two opposed lateral fields were used. The prescribed photon beam dose was depending on the type of tumor, in general for all cases is divided into 20 fractions using 6 MV photons.

Results: The comparison of 3D-CRT outcomes for all patients showed that the most common location of a tumor in the brain was in GBM in temporal and frontal parts of the brain and consist about 25% to total types of tumor in the brain for patients in this study, more than 62.5% of patients were treated with doses more than 4400 cGy the homogeneity index was better for patient No. 1 than other patients (0.0694). The mean dose for the Right lens was higher for patient No. 8 than for other patients was (1530 cGy). While in the left lens the mean dose was higher in patient No. 3 than in other patients was (1501 cGy), and the mean dose for both lenses in all plans for all patients was less than ≤10 Gy (the standard tolerance value). The highest mean dose received by the left optic nerve in patients number 2 was (3339 cGy), and the more mean dose received by the right optic nerve in patients number 2 was (3645 cGy), but in both two sides of the optic nerve the mean doses them less than ≤ 50 Gy the standard tolerance value. The mean dose received by Brain stem for all patients was less than ≤ 50 Gy tolerance dose. The mean dose received by Open Chiasm for all patients was less than ≤ 54 Gy tolerance dose

Conclusion: This study showed that 3DCRT spared the volume of the healthy tissue surrounding the brain tumor to be irradiated to achieve the most accurate treatment delivery to best planning target volume. The application of 3D-CRT was successful in justification of radiation dose to lower than tolerance dose in all evaluated brain tissues.

Keywords: 3DCRT, Dose Volume Histogram, Organs at Risk, Brain tumor

Background and objective

Radiotherapy is a technique that utilizes a very high energy photons beam to destroy malignant tumor cells. Radiotherapy is usually carried out by a linear accelerator.

Three-dimensional radiography (3DRT) is a therapy technique that delivers radiation dose to a target area. Beams of radiation by a machine directly target the tumor during treatment. The passing beams through the body will destroy both the cancer cells and normal tissues in their path.

The purpose of three-dimensional conformal radiation therapy (3D-CRT) is the maximum radiation doses to the tumor area while minimizing irradiation of normal surrounding tissues by accurately conforming the dose distribution to the target volume shape[1,2].

Radiation therapy is a therapeutic tool for the treatment of most malignant and a significant number of benign primary CNS tumors. Radiotherapy may be an important treatment if the brain tumor can't be extracted with surgery.

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*Corresponding Author: Fatiheea Fatihalla Hassan
Email: fatiheea.fatihalla@hmu.edu.krd

It's also may be used after surgery to treat any cancer cells that may remain in the area of treatment, and can sometimes be used if the tumor has returned after surgery.

The duration of treatment depends on the type and volume of the brain tumor, but it is usually 2–6 weeks, with five fractions dose per week. Some people will have different treatment plans and may have treatment on the only treatment duration of three days a week [3, 4].

In radiotherapy, radiation is delivered to achieve a therapeutic benefit within three major volumes when planning by using 3DCRT are as follows:

- The first volume is called the gross tumor volume (GTV), is related to the location and extension of the gross tumor.
- The second volume, which is called the clinical target volume (CTV), consists of GTV together with a margin of sub-clinical disease spread.
- Uncertainties in positioning and delivery require the use of a planning target volume (PTV) which allows the inclusion of uncertainties in treatment planning. This volume is a concept of geometry designed to ensure the actual delivery of radiotherapy dose to the CTV (2) (figure. 1).

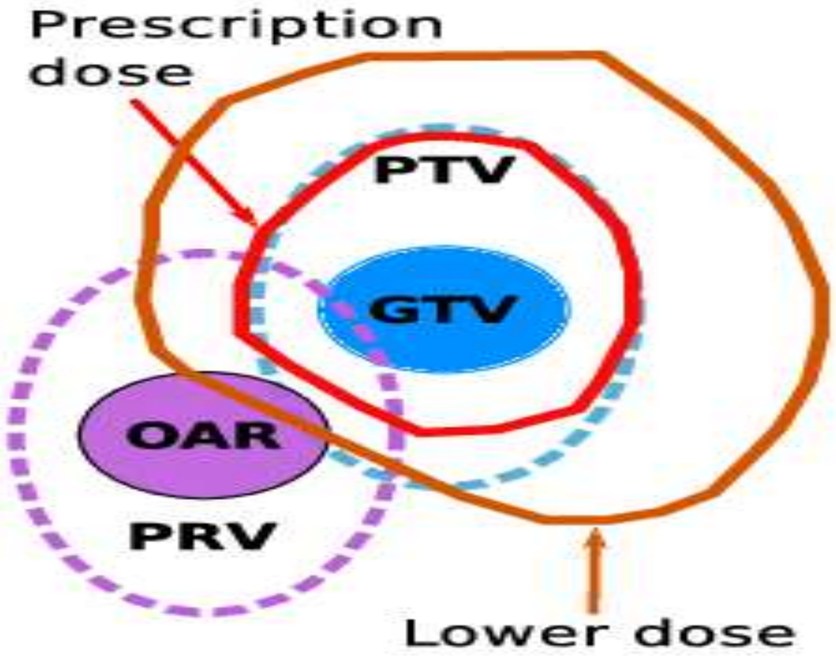


Figure 1. Organs-at-risk (OARs)

Organs-at-risk (OARs) refers to healthy surrounding tissue structures, which are at risk of being exposed to a dose of radiation. OARs should always be considered in radiotherapy planning[3].

With modern treatment planning systems, high-dose regions that include target area and field size within the radiation-beam path are typically well described. But, the precision of dose determinations outside the treatment field edge is usually poor, especially surrounding the cancer area.[2,3] in these cases, planning treatment techniques are used to assess the dose to the patient.

Healthy surrounding tissue will be exposed to low radiation doses outside the treated volume these low doses can cause deleterious effects to the patient. The risk of late effects and induce second cancer from secondary radiation may be more evident today after following up the number of cancer patients who survive and live long enough for understanding future radiation effects on healthy tissues to manifest. [4]

The dose outside the target area depends on field size, increasing with increasing field size because more diverging of the radiation beam, and larger irradiated volumes produce more patient scatter. This area dependence is most pronounced close to the field edge of the target, where patient scattered radiation is the most important component of the outside of field dose.

This study evaluates the dose distribution of planned conformal radiation therapy (CRT) of brain cancer for all patients and assesses its effect on target coverage and normal tissue sparing for cancer patients such as lenses of the eye, cochlea, open chiasm, and brain stem.

Method

The cases of 8 patients with different types of brain cancer were treated by using 3DCRT at Zhianaw center-Sulimani-KR. The planning for each patient had been performed using a CT scan with 3 mm slice separation, with conformation provided by MLC.

The PTV and OARs (lenses, cochlea, optic nerve, optic chiasm, and the brain stem) were contoured for each patient.

One 3D-CRT plan was produced for each patient. The plans used a unique isocentric technique with two 6-MV photon fields' lateral, plus one field vertex; a third field was added when required to compensate for variation in target thickness in the superior-inferior direction with different gantry angles between ((60-90) degree, and (240-270) degree).

The treatment plan for each patient was established by the use of an XIO planning system superposition algorithm, and 6 MV photon beams provided by an ELEKTA Synergy linear accelerator, equipped with a multi-leaf collimator (MLC), having 80-leaf with 1 cm width projected at the isocenter. Where necessary, the field size was increased at the superior and inferior ends to achieve adequate coverage of the PTV by the 95% isodose. Determined the prescription dose of radiation for each patient then divided the total dose to 20 fractions per 4 weeks, 2 Gy per fraction, 5 fractions per week, which satisfies most recommendations of the International Commission of Radiation Units (ICRU). A region that was clinically relevant to PTV and had a low dose gradient was selected as the reference point. In order to control dose homogeneity, some additional dose points in PTV were considered[5]. Each course of radiotherapy is planned according to the particular needs of each patient.

In this study, the maximum and minimum PTV dose limits, Dmax and Dmin, were those recommended in ICRU [6]

For each patient, The planning target volumes (PTVs), Gross tumor volume (GTV), and clinical target volume (CTV) were delineated. Organs at risk (OAR); the right lens of the eye, left lens of the eye, right cochlea, left cochlea, optic nerve, optic chiasm, and brain stem also were delineated for each patient.

The treatment plan for each patient was established by the use of an XIO planning system superposition algorithm. Each course of radiotherapy is planned according to the particular needs of each patient.

XiO planning system

Elekta's XiO has a great potency to provide a strong planning system for radiotherapy treatment. XiO is a good system for precision planning and fluent workflows and can satisfy your expectation of an Elekta treatment planning [7].

Dose description

Dose-volume histograms (DVHs) as well as isodose lines can be utilized to evaluate dose distribution. Therefore, finding fast and easyto-use tools with the ability to analyze dose distribution in treatment plans and facilitate the selection of an optimum plan which provides maximum homogeneous tumor coverage whilst protecting critical organs.

Results

Treatment was done on eight patients with different types of brain tumors radically treated in Zhianaw center- sulimani, KR (Iraq) between 2018 and 2019. The median age of the study population at diagnosis was 45 years (range: 25–65 years).

Table 1. the dosimetric plan comparison of all eight patients by using 3DCRT with locations of the tumors in the brain

No, of Patient	Location of cancer in the brain	TOTAL VOLUME cc	MIN DOSE cGy	MAX DOSE cGy	MEAN DOSE cGy	D98% cGy	D50% cGy	D2% CGy	Dose PTV cGY	HI
1	Pineal lesion with extension to both thalamus and pons	283.55	1527	1912	1838	1770	1837	1889	1800	0.0694
2	GBM Glioblastoma multiform	569.59	3520	4810	4540	4280	4555	4726	4600	0.102
3	Pons upper medulla and part of mi brain	288.39	2289	4158	3934	3643	3953	4095	3900	0.121
4	LT sided facial palsy	109.73	3060	4811	4526	4207	4534	4760	4500	0.129
5	Secretory macroadenoma	24.43	4404	5285	5138	4819	5176	5250	5040	0.09
6	Left sided carpus callosum	332.8	3592	4757	4457	4096	4469	4663	4400	0.135
7	GBM Glioblastoma multiforme	384.13	2144	2678	2511	2385	2519	2645	2500	0.109
8	RT optic nerve	81.85	4357	5314	5033	4764	5037	5291	5040	0.104

Max dose: Maximum dose received by a particular point; mean dose: Mean dose received by the organ, tumor volume and Dmax and Dmean were noted for all. Planning target volume PTV, For PTV, doses received by 98 and 2% volumes were also noted (D98 and D2). Mean dose, max. Dose and minimum dose were calculated. HI = homogeneity index, the mean HI were calculated., 3DCRT; three-dimensional conformal radiotherapy**.**

A summary of DVH analysis can be found in Table 1, where mean values over the cohort of eight patients are reported together.

As shown in Table 1, compared between the relative volume of PTV which was greater in patients with Secretory macroadenoma GBM, and Right (RT) optic nerve (5040 cGy), and it was lower in patient's Pineal lesion with extension to both thalamus and pons (1800 cGy). The volume of PTV receiving high (D98%) and low (D2%) doses (Gy). The PTV98% coverage values of >98% of the prescription dose, and D 2% coverage value equal 2% volume of the PTV.

The most common location of a tumor was GBM in temporal and frontal parts of the brain (25%), followed by the Pineal lesion with extension to both thalamus and pons, Pons upper medulla and part of the midbrain, LT sided facial palsy, Secretory macroadenoma, Left-sided carpus callosum, and RT optic nerve with (12.5%) for each one.

All patients were planned by 3DCRTwith a single isocenter using six (6 MV) photons. More than 62.5% of patients were treated with a dose of more than 4400 cGy, the rest received only 1838 cGy, 2511 cGy, and 3934cGy given their proximity to critical organs.

The homogeneity index (HI) was measured by (Equation (1)) and measures the dose homogeneity across the PTV. An HI value approaching zero indicates a more homogenous dose distribution within the PTV [8,9,10].

$HI=D2\%-D98\%D50\%$ (1)

Where D2% and D98% represent the doses to 2% and 98% of the PTV, respectively.

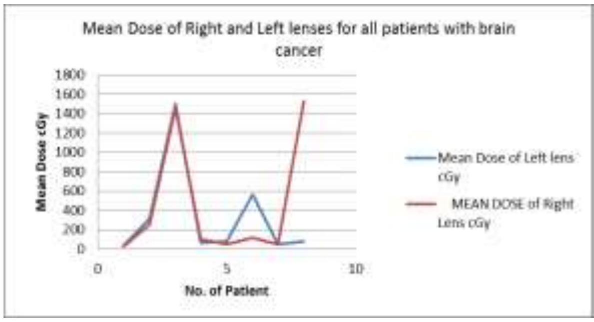
Equation (1) shows that lower HI values indicate a more homogenous target dose[10].

The more homogenous dose distribution in patient No. 1 with a tumor in the Pineal lesion with extension to both thalamus and pons HI was (0.0694), and less homogenous dose distribution among eight patients in patient No. 6 with a tumor in Left-sided carpus callosum HI was (0.135).

Table 2. define the location of tumor for each eight patients

No, of Patient	Location of tumor in the brain	define
1	A pineal lesion with extension to both thalamus and pons	It's a lesion that is somehow in the middle of the head(below parietal and behind frontal and medial to temporal and in front of the occiput)
2	GBM Glioblastoma multiforme	It's a type of cancer that's very aggressive and it can be anywhere in the brain but the most common locations are temporal and frontal parts of the brain mostly
3	Pons upper medulla and part of the midbrain	It's just above the spinal cord and below the brain and it can be described as the lower middle part of the internal head
4	Left-sided (LT) sided facial palsy	It's a nerve that starts in the pons and continues its root next to temporal areal of the brain and below parietal just to reach muscles in face and problem can happen anywhere along the path
5	Secretory macroadenoma	It's a lesion that is somehow in the middle of the head(below parietal and behind frontal and medial to temporal and in front of the occiput)and it just happens to be in front of the pineal body
6	Left-sided carpus callosum	Carpus callosum has a border with all brain part and its somehow in the internal medial border of them
7	GBM Glioblastoma multiforme	It's a type of cancer that's very aggressive and it can be anywhere in the brain but the most common locations are temporal and frontal parts of the brain mostly
8	RT optic nerve	It's most close to the frontal part

Table 2 shows the location of the tumor for each patient with a brief explanation of the type of tumor and its location in the brain.



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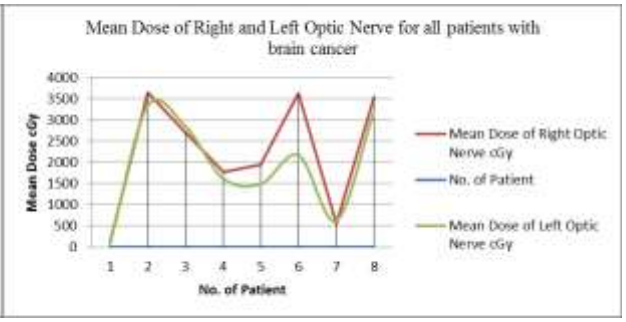

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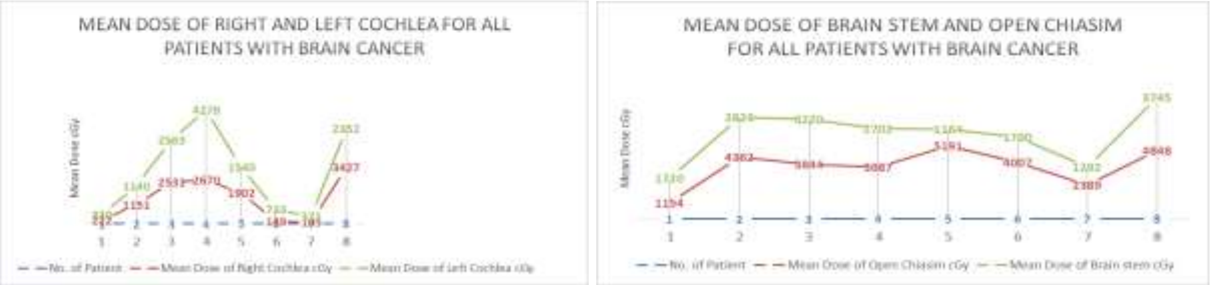

Figure 2. (a) Mean dose received by the left and right Lenses surrounding the target volumes. (b) Mean dose and maximum dose received by left and right optic nerve near the target volumes. (c) Mean dose and maximum dose received by Cochlear surrounding the tumor in the brain. (d) Mean dose and maximum dose received by Brain stem surrounding the tumor in the brain.

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As shown in Figure 1, the more mean dose received by right lenses in patients number 8, and 3were (1530, 1462 cGy, respectively) which tumors in Pons upper medulla and part of the midbrain, and RT optic nerve. And the highest mean dose received by the left lens in patient number 3 was 1501 cGy, which tumor located in Pons upper medulla and part of the midbrain. Both right and left lenses mean dose were less than Tolerance Dose value (≤ 10 Gy). (11)

The more mean dose received by the left optic nerve in patients number 2, 3, and 8 were (3339 cGy, 2849 cGY, and 3200 cGy respectively) which tumors in GBM Glioblastoma multiforme, Pons upper medulla and part of the midbrain, and RT optic nerve. And the more mean dose received by the right optic nerve in patients number 2, and 8 were (3645 cGy, and 3533cGy respectively) which tumor location in GBM Glioblastoma multiforme, and RT optic nerve.

In general, mean dose received by patients of Right optic nerve more than Left optic nerve because the tumor location its most close to the frontal part slop to right, but in both two sides of optic nerve the mean doses them less than ≤ 50 Gy tolerance dose [11]

The more mean dose received by left Cochlea in patients number 4, and 8 were (4278 cGy, and 2352 cGy respectively) which tumors in LT sided facial palsy, and RT optic nerve. And the more mean dose received by right Cochlea in patients number 4, and 8 were (2670 cGy, and 3427 cGy respectively) which tumor location in LT sided facial palsy, and in RT optic nerve.

In general, the mean dose received by patient 4 more than other patients because the tumor location which's a nerve that starts in the pons and continues its root next to temporal areal of the brain and below parietal just to reach muscles in face and problem can happen anywhere along the path and slop to left, both of them less than **≤ 40 Gy tolerance dose** [11]

The higher more mean dose received by Brain stem in patients number 8 and lower mean dose in patient number 7 was (3745, 1292 cGy respectively), which tumor was located in RT optic nerve for patient No. 8, and GBM Glioblastoma multiforme to patient No. 7. The mean dose received by Brain stem for all patients was less than **≤ 50 Gy tolerance dose** [11]

The highest mean dose received by open Chiasma in patient number 8 and lower mean dose in patient number 1 was (4848, 1154 cGy respectively), which tumors located in RT optic nerve for patient No. 8, and in the Pineal lesion with extension to both thalamus and pons to patient No. 1. The mean dose received by open Chiasma for all patients was less than ≤ 54 Gy tolerance dose value [10]

Discussion

Radiation therapy (3D-CRT) is a conventional method of radiotherapy in which X-rays are designed in a special order and arrangement to match the shape of the brain tumor and thus reach the maximum dose of radiation to the tumor and reduce the amount of radiation to healthy surrounding tissues to a minimum. This radiation procedure is designed to fit the patient's anatomy and the location of the tumor in the brain. CT scans and MRI scans are usually needed to plan and adjust this procedure.

The present study is a dosimetric study when applying 3D-CRT technique in the treatment of brain cancer. The results of our study indicate that the application of 3D-CRT was successful in justification of radiation dose to lower than tolerance dose in all evaluated brain tissues.

For certain critical tissues in this study, the delineation and the assessment dose restriction should be evaluated based on the tumor volume in the brain, tumor control, and size of organs at risk that are surrounding the target area.

In all patients and according to this study results by using 3DCRT, the volume of healthy tissues inside the planning target volume (PTV) may be portrayed separately and dose limitations may be aimed for each healthy tissue surrounding the brain tumor.

A study by Chan et al[12] that was performed to evaluate the Intensity-modulated radiation therapy (IMRT) method by designing an adaptive 3D -CRT in GBM tumors. In the 3D-CRT method, a photon with an energy of 6 MV was used. The results of their study confirm the significant superiority of the IMRT method in cases where the tumor is located near critical organs such as the brainstem. While using 3D-CRT in their study had also beneficial effects, as well as seen in our study.

Several other studies have compared 3D-CRT treatment design methods and IMRT in the treatment of GBM tumors, all of which emphasize the effectiveness of the IMRT method.

A study by Panet-Raymond et al. Examined the treatment of IMRT using planar and non-planar radiation for GBM tumors[13]. The treatment design of these patients in one stage of treatment was designed according to the procedure of 26052-22053 European Organization for Research and Treatment of Cancer (EORTC)[14].

IMRT method, like 3DCRT, links CT scan images to the designed software, which makes it possible to view cancerous areas in three dimensions. However, 3DCRTs and IMRTs differ in the pattern and volume of radiation emitted to the body. In the conventional 3 DCRT, radiation patterns are given to the computer. At IMRT, the specific doses that the tumor and surrounding healthy tissue should take, could be determined. While in our study we hadn't infrastructure of using IMRT due to limitations of our medical center but we recommend this comparison in further studies.

Lorentini et al.,[15] showed that IMRT is superior to 3D-CRT. Their study determined criterion for the selection of patients to receive IMRT or conventional 3D-CRT.

In the study of Ding et al.,[16] they showed that 3D-CRT is suitable for small targets when IMRT was not effective. in larger tumors, IMRT showed a better response than 3D-CRT.

In our study, the PTV98% coverage values of >98% of the prescription dose, and D 2% coverage value equal 2% volume of the PTV. This result corresponds with Abo-Madyan et al. study results[18].

With the most modern technologies of radiotherapy, not all of the dose limitations might not be completed due to the characteristic of the photon beam. The organ at risk should always be given precise dose restrictions. If the PTV is overlapping with such structures, underdose of radiation the area is accepted.

Conclusion

3DCRT allows for the most accurate treatment delivery with rising of PTV dose and different fractionations that can improve target control while protecting healthy tissues through reducing the volume of healthy tissue irradiated to high doses of radiation, and, hence, minimizing the long-term toxicity of radiation treatment or induce second cancer in the future as a result of exposure to a low dose of radiation during radiotherapy.

Conflict of Interest Disclosures

The authors declare that they have no conflicts of interest.

Authors' contributions

FFH wrote the first draft of the article and collected data; NKA managed the writing of the last version and helped in the design of the study; IKI edited the article and helped in the statistical analysis; DKI helped to the draft manuscript. All authors approved the last version of the manuscript**.**

Abbreviation

Abbreviation	Explanation
3DCRT	Three-dimensional conformal radiotherapy
PTV	planning target volume
OARs	organs at risk
Gy	Gray
GBM	Glioblastoma multiform
GTV	Gross tumor volume
CTV	Clinical target volume
CT	Computed Tomography
MLC	Multi-leaf collimator
ICRU	International Commission of Radiation Units
Dmax	Dose Maximum
Dmin	Dose Minimum
DVHs	Dose-volume histograms
KR	Kurdistan Region
HI	Homogeneity Index
LT	Left-sided
MRI	Magnetic Resonance Image
IMRT	Intensity-modulated radiation therapy
EORTC	European Organization for Research and Treatment of Cancer

Ethical Approval

The present study was conducted following the approval by the Ethical Committee of Hawler Medical University (KR, meeting code: 9, paper code: 2, date: 11/10/2020)

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