Improving accuracy and safety
in
image-guided keyhole neurosurgery

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by

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Abstract

Image-guided keyhole neurosurgery consists of targeting a straight surgical tool, such as a needle or a catheter, with a support guidance system towards a target location inside the brain. The target and trajectory are defined on a preoperative MRI/CT image before the surgery. In the operating room, the support system facilitates the alignment, called registration, of the preoperative image and plan with the physical location of the head, and supports the accurate execution of the preoperative plan. Instrument misplacement may result in ineffective treatment or severe neurological complications, and therefore it is important to study and improve the accuracy and safety of these systems.

We have developed novel methods for estimating and improving accuracy and safety in image-guided keyhole neurosurgery. A key characteristic of our work is that it considers both theoretical and clinical-experimental aspects of image-guided keyhole neurosurgery that eventually evolved into a comprehensive study yields important clinical insights. The thesis is organized as follows. At first, we introduce image-guided keyhole neurosurgery procedures, the support systems, and formulate our research goals. Next, we study the actual application accuracy in keyhole image-guided neurosurgery. The most clinically relevant error measure is the Target Registration Error (TRE), which is the distance between the image-defined target and the corresponding target on the physical head after registration. Since targets are intracranial, the TRE has to be estimated. Two common estimation measures are the Fiducial Registration Error (FRE), which is the root mean square distance between the fiducials in both data sets after registration, and Fitzpatrick's TRE (FTRE) formula. We have measured and characterized the surgical tool localization accuracy in the operating room and in-vivo. One result of our study is that the measured FRE and FTRE are not always good estimators of the TRE. Then, we present a theorem shows that both: FRE and FTRE are uncorrelated with the actual TRE in some realistic situations. Next, we propose two methods for improving image-to-patient registration accuracy. The first method is using a fast, high resolution facial surface scanner acquires tens of thousands of points, and the second method is computing optimal registration-points locations. Both methods were tested in the operating room in-vivo. Finally, we present a new method for assisting the neurosurgeon in defining the safest trajectory. The method was tested in a clinical setup and improves safety.
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Chapter 1: Introduction

Neurosurgery is an invasive operation of the brain, spinal cord or peripheral nerves aimed at treating neurological disorders [1]. The invasiveness level of the operation is directly related to the expected risk [2] such that open skull brain surgeries are associated with higher complications and mortality rates than those executed via a small incision, called keyhole. Keyhole neurosurgery consists of targeting a straight surgical tool, such as a needle or a catheter, towards a target location inside the brain. Typically, the target location and tool’s trajectory are defined on preoperative images and aligned with the patient’s head in the operating room using a support system. This alignment is called registration. After registration, the system supports the accurate execution of the planned surgery [3]. In unpublished survey we have conducted, we estimate the number of image-guided keyhole neurosurgeries at Israel as 4,000. We estimate the number of image-guided keyhole neurosurgeries in developed countries as 500,000, assuming that the ratio between the population size and the number of surgeries in developed countries is similar to that of Israel.

A misplacement of the surgical instrument may result in undesired complications such as non-diagnostic tissue samples, ineffective treatment, intracranial hemorrhage, and temporary or permanent neurological damage. The complications are often followed by another procedure with a similar goal to that being missed or by open-skull emergency operation aimed at minimizing the hazard. The additional operation is bounded with additional risk to the patient. Therefore, it is important to study and improve the accuracy and safety of these systems [4-7].

This chapter is organized as follows. In Section 1.1, we briefly describe image-guided keyhole neurosurgery procedures and characterize their commonalities. In Section 1.2, we outline a typical workflow of these operations. In Section 1.3, we describe four support systems that facilitate the implementation of these operations. In Section 1.4, we pose key questions regarding these systems and present our research goals. In Section 1.5, we present an overview of this thesis. In Section 1.6, we describe our contribution novelties. In Section 1.7, we present the thesis organization.
1.1 Clinical Procedures

Image-guided keyhole neurosurgeries have four important common properties [8]:

1) They are minimally invasive surgeries (MIS), performed via a keyhole of 3-30mm diameter opened on the skull.
2) They require precise targeting and mechanical guidance support.
3) The targets and entry points are determined preoperatively on the CT/MRI image.
4) It is assumed that little or no brain shift occurs during the MIS.

Next, we briefly describe the most common image-guided keyhole neurosurgery procedures.

Brain biopsy
Brain biopsy is the gold standard for accurately determining tumor pathology. It consists of harvesting, with a hollow needle a tissue sample, from a predefined target site within the brain so it can be analyzed in the pathology laboratory. Biopsies are usually done making a small opening (3-14mm burr hole) in the skull and carefully introducing a biopsy needle with a support guidance system.

Hydrocephalus treatment
Treatment of congenital or acquired hydrocephalus is indicated for alleviating the abnormal accumulation of cerebrospinal fluid (CSF) within the brain ventricles. It consists of diverting the flow of fluid away from the ventricles by inserting a shunt. A valve in the shunt maintains the CSF at a normal pressure and volume within the ventricles.

Hematoma evacuation
Evacuation of hematoma is a surgery used to reduce intracranial pressure caused by an expanding bleeding resulting from head injury stroke, or bleeding into a tumor. The goal of the surgery is to decrease morbidity and mortality and to relieve neurological symptoms. It consists of placing an aspiration needle in the hematoma and aspirating the blood out.
**Ommaya catheter insertion**

‘Ommaya’ catheter insertion surgery is indicated for the on-site repeated delivery of drugs (e.g., chemotherapy and antibiotics) to the ventricular system. It is also performed for repeated CSF sampling and to evacuate cystic lesions in the brain when surgical excision is not appropriate. The surgery consists of inserting a silicon catheter into the ventricles or cystic cavity. The catheter is connected to a small silicon reservoir (the ‘Ommaya’ reservoir) implanted under the scalp so that the reservoir can then be easily approached with a needle puncture through the scalp.

**Deep brain stimulation**

Deep brain stimulation (DBS) is a procedure for effectively treating certain types of Parkinsonism, primary tremor, dystonia, hemibalismus, and thalamic pain. It consists of implanting, through one or more small skull openings, electrodes into specific targets of the brain and providing electric stimuli to these locations.

**Minimal access craniotomy**

Minimal access craniotomy is performed to resect deep brain tumors, vascular malformations, and brain abscesses. It consists of opening a small circular hole (20-30mm radius) in the skull and introducing a surgical instrument reach the area of interest.
1. **Pre-operatively**

1a. Pre-imaging preparation – implant skull screws and/or attach skin markers.
1b. Image acquisition – acquire a CT/MRI image.
1c. Planning – elaborate the pre-operative plan and identify targets and entry points.

2. **Intra-operatively**

2a. Preparation – set up the support system and perform patient preparation.
2b. Registration – align the preoperative plan and image with the physical head.
2c. Localization – locate the entry point with a tracked tool and perform incision.
2d. Guidance – provide mechanical guidance for the needle/probe insertion.
2e. Insertion – insert the needle to a planned depth at the proper speed/force.
2f. Repeat steps 2b-e as necessary.

| Table 1: Typical keyhole image-guided neurosurgery protocol. |

### 1.2 Keyhole neurosurgery workflow

All clinical procedures follow a similar surgical workflow that is described in Table (1) [8]. Preoperatively, markers for image-to-patient alignment can be attached to the patient’s head (1a). Then, the patient head is imaged (1b) and the neurosurgeon selects the preferred target and entry point (1c). In the operating room, after full general anesthesia is administered, the patient’s head is usually fixed in a head-holder to the surgical table and the support system is installed (2a). Then, the head image is aligned (e.g. registered) with the actual patient head (2b). Then, the neurosurgeon localizes the entry point and makes the burr hole (2c). A mechanical guidance is installed and adjusted to support tool’s insertion (2d), and then, the operation is performed (2e). If undesired complication has occurred, steps 2b-e can be repeated as needed.

### 1.3 Support Systems

Four types of support systems for image-guided keyhole neurosurgery are currently available: 1. stereotactic frames; 2. navigation systems; 3. robotic systems, and; 4. interventional imaging systems.
Figure 1: A stereotactic frame: preoperative (a) and intra-operative (b) setups.

Stereotactic frames
Stereotactic frames (Figure 1) provide precise positioning with a manually adjustable frame rigidly attached to the patient skull [3, 9]. Prior to image acquisition, four frame position screws are implanted in the patient’s skull. An imaging coordinate box, called indicator, is mounted on the frame and the patient is scanned with it. The surgeon identifies the brain targets and entry points on the images and computes the corresponding stereotactic frame coordinates based on the imaged indicator. Intra-operatively, the stereotactic frame is adjusted according to the computed coordinates and mounted on the immobilized patient skull at the implanted screws. Keyhole surgery of the skull opening is then done. Optionally, a linear drive needle insertion guide is mounted on the frame to automate needle insertion and retraction.

The advantages of the stereotactic frames are: 1) it is the current standard of care, has been extensively used, and has been clinically validated since their introduction in the 1970s; 2) frames are relatively accurate (≤ 2mm of the target) and provide rigid support
and guidance for needle insertion, and; 3) they are relatively inexpensive (US$50-100K) compared to other support systems. Their disadvantages are: 1) they require the preoperative implantation of the head screws under local anesthesia; 2) they cause discomfort to the patient before and during surgery; 3) they are bulky, cumbersome, and require manual adjustment during surgery; 4) they require patient head immobilization during surgery; 5) selecting new target points during surgery requires new manual computations for frame co-ordinates, and; 6) no real-time feedback of the needle position is provided.

Navigation systems

Navigation systems (e.g., Medtronic, USA and BrainLab, Germany) show in real time the location of hand-held tools of the pre-operative image onto which targets have been defined (Figure 2) [3, 10-13]. The registration between the preoperative data and the patient is performed via skin markers affixed to the patient’s skull before scanning, or by acquiring points on the patient’s face with either a laser probe or direct contact. A manually positioned tracked passive arm (e.g., Phillips EasyTaxis™ or Image-Guided Neurologics Navigus™) provides mechanical guidance for targeting.

Figure 2: A navigation system facilitates (a) the manipulation of a tracked surgical tool with (b) real-time localization feedback on the preoperative patient’s head image.
Since nearly all navigation systems use optical tracking, careful camera positioning and the maintenance of a direct line of sight between the camera and tracked instruments is required at all times.

Their disadvantages are: 1) their high cost (US $150-200K); 2) they require head immobilization; 3) they require the maintenance of a line of sight between the camera and the instruments, and; 4) they require manual passive arm positioning, which can be time-consuming and error-prone; The main advantages of navigation systems are: 1) they provide continuous, real-time surgical tool location information with respect to the defined target; 2) they allow the selection of new target points during surgery; 3) they are quickly gaining wide clinical acceptance since their introduction in the early 1990s.

**Robotic systems**

Robotic systems (Figure 3) provide frameless stereotactic neurosurgery with a robotic arm that automatically positions itself with respect to a target defined in the preoperative image [14, 15]. They have the potential to address intra-operative localization, guidance, and insertion with a single system. The registration between the pre-operative image and the intra-operative situation is done by direct contact or with video images. Two
floor-standing commercial robots include the NeuroMate™ (Integrated Surgical Systems, USA – now defunct) and the PathFinder™ (Armstrong HealthCare, UK).

Their disadvantages are: 1) they are usually bulky and cumbersome; 2) they pose a potential safety risk due to their size and weight; 3) they require head immobilization or real-time tracking; 4) they are costly (US $300—500K); 5) they are not commonly used, with only a dozen systems currently deployed. Their advantages are: 1) they provide a frameless integrated solution; 2) they allow intra-operative plan adjustment, and; 3) they are rigid and accurate.

**Interventional imaging**

Interventional imaging systems (Figure 4) produce images showing the actual needle/probe position with respect to the brain anatomy and target [16]. A few experimental systems also incorporate real-time tracking (Stereotaxis, Inc) and robotic positioning devices. The main advantage of these systems is that they provide up-to-date images that account for brain shift (a secondary issue in the procedures we are considering), and needle bending. The main drawbacks are: 1) their limited availability; 2) they are cumbersome and the intra-operative image acquisition is time-consuming; 3) they have high nominal and operational costs, and; 4) for intra-operative MRI, complete expensive room shielding is required.
1.4 Research goals
We pose three key questions regarding the above support systems:
- What is the clinical application accuracy?
- How to improve image-to-patient registration accuracy?
- How to improve the safety of the systems?

What is the clinical application accuracy?
The most clinically relevant localization error measure is the Target Registration Error (TRE), which is the distance between the image-defined target location and the corresponding target in the physical head after registration [10]. The TRE has been extensively studied [10, 13-15, 17-25], but only few have measured it in-vivo in the actual clinical setup. Understanding the actual clinical application accuracy is important and useful for better estimating the possible tool misplacements, and for better evaluation of optional risks. The TRE directly depends on the Fiducial Localization Error (FLE), which is the discrepancy between the selected and the actual fiducial (e.g. a point used for registration) locations. Characterizing the actual FLE provides the solid basis for forthcoming more accurate image-to-patient registration methods, and for a better estimation of the TRE. Since the actual locations of targets usually cannot be measured after registration, the TRE is often estimated by the Fiducial Registration Error (FRE), which is the root mean square distance between the fiducials in both data sets after registration, or with the TRE estimation method suggested by Fitzpatrick et al. (FTRE) [26]. One goal of this study is to investigate the TRE, FTRE, FRE and FLE and analyze the actual relations between them by means of empirical-clinical experiments and a theoretical framework.

How to improve registration?
The image-to-patient alignment method, called registration, greatly affects the application accuracy of the support systems. Registration methods differ from each other by hardware, algorithms, and the internal parameters setup. Hardware includes one or a combination of: 1) skull mounted screws and/or custom mechanical devices used in stereotactic frames and less frequently in robotic and navigation systems; 2) a tracked
probe and skin adhesive markers for point based registration used in navigation and robotic systems; 3) surface scanner for facial surface registration used in navigation and robotic systems, and; 4) intra-operative imaging device to align pre- and intra-operative images used in interventional imaging, and less frequently in navigation and robotic systems. Algorithms for computing the registration between pre- and intra-operative datasets have been investigated for a long time [13, 17, 27, 28]. The methods differ from each other in their mathematical approach, the measure they minimize, and the assumptions they make regarding the input data and its characteristics. Usually, the internal parameters configuration is significantly affecting the registration outcome. For example, the accuracy of closed-form point-based registration methods is related to the specific locations of points. Reducing the actual TRE and improving the registration accuracy is another goal of us.

**How to improve the safety of the systems?**

Two additional factors that are affecting the operation risks are: 1) the selected trajectory and target, and; 2) localization inaccuracies during execution of the surgery that are not related to the registration error. A trajectory passing near a major blood vessel towards a deep located target, for example, is associated with a high risk and the neurosurgeon need to decide if the situation of the patient justifies the operation risks. In such complicated cases, the neurosurgeon may be interested in inspecting additional trajectories. Assisting the neurosurgeon selecting a safer trajectory is our last goal. During execution of the surgery, additional tool localization inaccuracies may occur. Although we did some studies to improve execution intuitiveness and accuracy [6, 29] this issue is outside the scope of this thesis.

**1.5 Thesis overview**

We have developed novel methods for estimating and improving accuracy and safety in image-guided keyhole neurosurgery [10, 17, 30-33]. A key characteristic of our work is that it considers both theoretical and clinical-experimental aspects of image-guided keyhole neurosurgery that eventually evolved into a comprehensive study yields important clinical insights.
Specifically, we show in a clinical study that the FRE and FTRE values are not indicating the actual TRE and may be significantly smaller [10]. We characterize the image and physical FLEs, and provide a full account of the overall localization errors in a clinical setup. We then present a theoretical framework that supports these observations and explains long-standing conjectures [33]. Then, we describe new methods to improve surgical tool placement accuracy and patient safety. The methods include optimal fiducial selection and placement for point-based registration [32], tool trajectory risk estimation and optimization [30, 31], and robust surface-based registration [17]. The methods were tested in-vivo and under the full clinical setup, and significantly improved the accuracy and the safety of the systems.

1.6 Novel aspects
We present a comprehensive study incorporating clinical in-vivo experiments, a novel theoretical framework, and technical methods to improve the accuracy and safety in image-guided keyhole neurosurgery. Our analysis of the FLE and its effect on the targeting accuracy in the clinical setup facilitates forthcoming methods for a better estimation of the TRE. Moreover, we show on clinical data and in-vivo that the FRE and FTRE values are low correlated with the actual TRE. We have developed a theoretical framework shows that for some realistic situations the FRE and FTRE are indeed uncorrelated with the TRE and it may explain our clinical observations. The presented theorem is geometrical and significantly different from previous works used a statistical approach, and it may open a new direction for further studies on accuracy.

Our study on surface-based facial scan registration was the first to use high-resolution 3D optical surface scanner in the actual clinical setup and in-vivo. Another contribution of us is the estimation of registration error distribution at the entire image volume, compared to the few locations in previous surface-based-registration studies.

Our method for optimal markers placement and anatomical landmarks selection is based on a novel empirical method for TRE estimation and allows the convenient editing of the registration points with estimated TRE feedback. The method was tested in a clinical setup in-vivo, and demonstrated a significant improvement in targeting accuracy. In
addition, we suggest a global-optimum method as opposed to the local-optimum computed in previous studies.

Our method for minimal-risk path planning, jointly designed with the neurosurgeon, facilitates a convenient selection and editing of safe trajectories with a visual and quantitative feedback. This method is unique in its visualization module, its risk formula, the updated quantitative feedback interface, and in incorporating tool localization uncertainty model. Moreover, a neurosurgeon tested the method on clinical data and it was shown that trajectories planned with our method are safer than those planned with the routine method. The experiment is also unique and poses higher standards than that of previous works.

1.7 Thesis organization
The thesis is organized as follows. In Chapter 2 we investigate the clinical application accuracy under the full clinical setup on patients underwent keyhole image-guided neurosurgery [10]. One important result of our study is that two commonly used measures: the FRE and FTRE are not good estimators for the actual TRE. In Chapter 3 we develop a new theory that shows that the FRE and FTRE are uncorrelated with the actual TRE in some realistic situations and may explain the observations of Chapter 2 [33]. In Chapter 4 and Chapter 5, we investigate two directions for improving image-to-patient registration: 1) using a high resolution, fast and accurate facial surface optical scanner that has the potential of better accuracy as it acquires tens of thousands of points compared to the tens of points measured with the commercial systems [17], and; 2) computing and editing optimal markers placements and anatomical landmarks selection such that the TRE is minimized and considering empirical data [32]. Both methods were tested in the operating room in-vivo.

In Chapter 6, we present a new preoperative planning method for reducing the risk associated with insertion of straight tools in image-guided keyhole neurosurgery [30, 31]. The trajectory risk is evaluated based on the tool placement uncertainty, on the proximity of critical brain structures, and on a predefined table of quantitative geometric risk measures. Our clinical results show a significant reduction in trajectory’s risk as compared to the current routine method.
Chapter 2:
Localization and registration accuracy in image guided neurosurgery: a clinical study
Chapter 3:

Worst-case analysis of target localization errors in fiducial-based rigid body registration
Chapter 4:
Surface-based facial scan registration in neuronavigation procedures: a clinical study
Chapter 5:

Optimal landmarks selection and fiducial marker placement for minimal target registration error in image-guided neurosurgery
Chapter 6:

Trajectory planning method for reduced patient risk in image-guided neurosurgery: concept and preliminary results
Chapter 7: Discussion and conclusions

Image-guided keyhole neurosurgery is the method of choice for targeting tumors and anatomical structures inside the brain. Instrument misplacement may result in ineffective treatment and/or severe neurological complications, and therefore it is important to study and improve support system accuracy and safety.

In Chapter 2, we presented a clinical study that shows that the actual surgical tool placement error may be significantly larger than the estimation reported by commercial navigation systems and by analytic estimators. We characterize the image to physical registration errors, and provide a full account of the overall localization errors in a clinical setup.

In Chapter 3, we presented a theoretical framework that supports these observations and explains long-standing conjectures.

In Chapter 4, we examined a high resolution and accurate surface scanner for patient-to-image registration in the operating room and in-vivo. We found that its accuracy is clinically acceptable only for the frontal parts of the brain. This is because of the inhomogeneous spatial distribution of the registration error. In the frontal parts, the surface-based registration accuracy is comparable to that of using adhesive markers.

In Chapter 5, we presented a method for the selection of anatomical landmarks and placement of one marker that significantly improved the registration accuracy with respect to a predefined target (e.g. TRE). The TRE was estimated using a custom Monte-Carlo simulation that is based on empirical data.

In Chapter 6, we presented a novel method for assisting the neurosurgeon in selecting a safe trajectory. The method presents the neurosurgeon the risk information in a convenient way and allows the easy adjustment of the trajectory or comparing several trajectories with a visual and quantitative feedback. Our study shows significant improvements in the safety of the selected trajectory and in planning time for some of the patients.
We discuss now several ways for improving the accuracy and safety in image-guided keyhole neurosurgery. Previous works suggested to improve accuracy using skull or skin mounted markers [20]. However, note that markers do not always lead to a clinically significant accuracy improvement [10]. Moreover, adhesive markers are sometimes associated with patient discomfort and may fall or shift because of mishandling. Surface-based registration is associated with registration errors that are similar to that of anatomical landmarks [20]. Another option is to compute the optimal markers locations and the best anatomical landmarks subset [32, 34]. These methods show the neurosurgeon what anatomical landmarks to choose and where to place the markers based on the diagnostic images and with respect to the target location. Our experiments in Chapter 5 show a significant improvement in the accuracy of tool localization. Moreover, new point-based registration methods that incorporate a more realistic FLE models have the potential to better estimate the patient-to-image transformation [35, 36]. As for improving the evaluation of the expected accuracy, recent TRE estimation methods also incorporate more realistic FLE models and have the potential of better estimating the actual TRE [18, 37]. Yet, none of the recent or previous methods was validated in a realistic clinical neuronavigation setup.

We are currently developing an uncertainty geometric model that is based on the measured errors and that can be used for the evaluation of possible surgery outcomes. Methods for the computation of trajectories that are in a safe distance from critical structures reduce the risks associated with tool misplacement in neuronavigation as we have shown in Chapter 6. The methods automatically compute the risks along tens of thousands of candidate trajectories and present them to the neurosurgeon for further refinement. Methods to improve the accuracy and safety of the trajectory and target localization should be further developed and examined under a clinical setup.

**Future work**

Following our research, we foresee the development of new methods for assisting the neurosurgeons in planning and performing keyhole neurosurgeries. A new concept we are currently developing is “closed-loop feedback surgery”. That is, assuming that the localization errors are measured routinely after every surgery, the support system will
“learn” and compensate the neurosurgeon errors. Advanced military cannon positioning systems compensate the gunner bias successfully and we hope to merge this technology into medicine. In addition, routine localization error feedback will allow presenting in the planning stage the expected tool misplacement based on past observations.

Further studies on accuracy should be conducted testing new hardware, methods and internal parameters configurations. Since different neurosurgeries have different characteristics and are associated with different accuracy requirements, tailored planning and registration methods can be developed with the aim of better accuracy and safety. For example, Deep Brain Stimulation (DBS) of the Sub Thalamic Nucleus (STN) is used to treat Parkinson disease patients that are not well responding to drugs. DBS is characterized with a trajectory that is passing near similar cranial structures and the required accuracy is high (~1mm). As opposed to patients with other disorders, the geometry of brain structures is similar visually to those of the normal brain. Moreover, the path is selected from a small sub-volume of the image. In this case, it may be possible to easily segment critical structures semi-automatically, to suggest optimal paths and to develop a tailored registration setup and protocol such that the localization error at the target is minimized.

Another challenge is to extend our study for open skull neurosurgeries where brain shift usually occurs and significantly complicates the operation. Methods for compensating brain shift are under study, but no real-time deformable registration method is used routinely in the operating room and till has to be developed.

Undoubtedly, new tools and methods will soon appear in image-guided neurosurgeries to foster safety and improve accuracy. We hope that our research will serve as a catalyst towards the development of these aids.
References


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הספר לא miệng הטובה ומריו פרנקו לפילוסופיה

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הוגש לפנים האוניברסיטת העברית, ירושלים

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ניתוח ראש מわかת התמונה הוא סכינית ייעילה אשר מאפשרת מגוון טיפולייםustria, שארבת ידimmון וחרום מ’hוים, מתן תורמת ייוודע להחל מחות רציוניות. תיפול יארקצון בברוח עקריתCTR ו-MRI, על הח蓰ים המדיפורים ל’nן מקורות,ם אמפרושות הigrants ל’על ביאופר מודיק

תבנית קוד ניווט שובא עלי התמונה. מסקר שערכנו, ונח מעריצים כי בישאר יבלע תריכים

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אנו פיתחנו שטוח לשער לשלוף את הדיק והבטיות של ומגרות אלה. יישנות שיוודית

בשולב הצה החרואות ושיטה חישובית עם עד הנברך קולנילק.

בפרק הדראון noreferrer כאולק וראש התוחמה של נרוכזריז הגונות התמנה, מתאריםكبرות את

התיפולים ויצירתיים המבקרות שעשתו, ומנים את המגדלים והשותות התוחמות

ובנחתים אל. לאחר מון, אף מגדרים את מסורות התמחות ורגים בחרודות של עבדה של

בפרק 2ו תרים את הדיק של מגרות יוטה רופאית בהנהא קולנילים מ’ליאס על

מקהלים. תוצרת השבחול של מחזור זה היא שישים מדריסים שלפוקולול לתשמחה בדם כר,

לאಮוד את דיק הממערות זאנס אמיונים. בפרק 3אי ממוחת האוריינית והדשה אושר מצא

שהמשתת מדידות עד’לא אישים שיוודים לאנש במדיציות ריאליים מבקדים אחר

הנחתולים שוקulings בפרק 2. בפרק 4ו 5 אוג התרומץ שטי רכיבים לשייווד הדיק של יהודי

תמותת ראש התמולים עם מקורות הפש: 1(עיין פש.) הפיכת הפנים עורץ סרוכ מישتوز ודופי

בעל היפולציה רדיק גבומיה אשי רכש שערוראל קוקרוע על המשה. 2(עיין הדרוי)

(יוואליציה) של הקובצת הנוקדה אופסיומיל אותה יצור בגרות ההאזכים ב’yתameleon ראש התמולים

ל’nן מקורーム בפצל. שטי השופטונבגרעלמטוילשובדHDR. בפרק 6אי צרお得

נוהים שמיעת המסריעת ולהנהגה ל’yנקה את המקולילользоватו בוחר כדי להמנוע מפגיעות

באורות קרישים ציל ימי.