

Three-dimensional Robotic-assisted Endomicroscopy with a Force Adaptive Robotic Arm

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Abstract—Effective *in situ*, *in vivo* tumour margin assessment is an important, yet unmet, clinical demand in surgical oncology. Recent advances in probe-based optical imaging tools such as confocal endomicroscopy is making inroads in clinical applications. In practice, maintaining consistent tissue contact whilst ensuring large area surveillance is crucial for its practical adoption and for this reason there is a great demand for robotic assistance so that high-speed endomicroscopes can be combined with autonomous scanning, thus simplifying its incorporation in routine surgical workflows. In this paper, a cooperatively controlled robotic manipulator is developed, which provides a stable mechatronically-enhanced platform for micro-scanning tools to perform local high resolution mosaics over 3D undulating moving surfaces. Detailed kinematic and overall system performance analyses are provided and the results demonstrate the adaptability in terms of both contact force and orientation control of the system, and thus its simplicity in practical deployment and value for clinical adoption.

I. INTRODUCTION

In cancer surgery, there is an increasing demand for intra-operative tissue assessment and tumour margin identification. Histopathological examination is still the “gold standard” but is a discrete, invasive process and the results are available typically in 1-2 weeks after the operation. Other techniques, such as cryosection, assist in generating the results sooner but they are still not real-time as they take a significant amount of operating time to be prepared. Usually, it takes more than 20 minutes, and suffers from reliability issues due to freezing artefacts. Advances in fibre optic technology, miniaturised optics and mechanics enable the acquisition of high resolution images at a cellular level *in vivo* and *in situ*, a process known as optical biopsy. Optical biopsy techniques, such as confocal laser endomicroscopy [1], and endocytoscopy [2] combined with flexible endoscopes or minimally invasive surgical instruments provide *in vivo* real-time morphological details about the tissue under examination.

These probe-based endomicroscopes present several significant limitations that hinder their clinical adoption. Manipulating these miniature fibre bundles (typically < 3 mm) with a manual instrument is challenging, as well as maintaining sufficient contact while imaging within deformable tissue structures and cavities. This is amplified by the demand for wide surface area scanning as the interpretation of individual

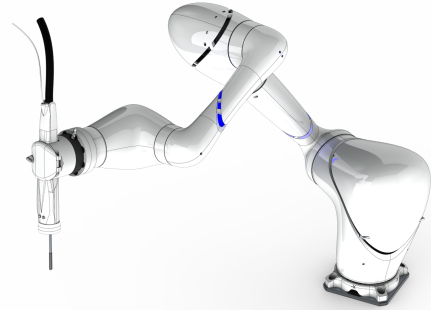


Fig. 1. Hamlyn Arm with a micro-scanning robotic tool.

microscopic images is not adequate for histology-like assessment and tissue interpretation [3]. High-resolution fibre bundle endomicroscopes have limited field-of-view (FoV) in the order of 240 μm , a size not comparable to large high-resolution histology images, making the surveillance of mm-scale areas challenging. Mosaicking techniques have been developed to increase the FoV of individual images, *i.e.* stitching adjacent image frames together as the probe moves across the tissue surface [4]. However, mosaicking is a partial solution to the effective scanning over large areas of complex tissue surfaces as the operator is required to maintain perpendicular probe pose and tissue contact while performing sub-millimetre scanning motions.

Robotic-assisted manipulation of the imaging probe has been explored recently to provide stable, precise, and consistent operation in comparison to manual manipulation [5]. Capabilities such as motion scaling, precise and tremor-free positioning, and advanced force sensing present robotic-assisted endomicroscopy as an ideal candidate to alleviate the limitations of endomicroscopic techniques and showcase the advantages of optical imaging in the operating theatre.

Initially, the importance of maintaining tissue contact to obtain good quality microscopic images was demonstrated in the early works of Latt *et al.* [6], [7] that developed hand-held one degree-of-freedom (DoF) active force controlled instruments. Load cells were used to sense forces applied axially to the tissue (distally [6] and proximally [7]) and linear actuation was used proximally to maintain consistent tissue contact at 100 mN (voice coil [6] and DC-servomotor [7]). Both works showcased the effects of forces on image quality of individual microscopic images, but not in terms of mosaicking or large area scanning. The latter was explored

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in the work of Giataganas *et al.* [8] where a cooperative robotic manipulator was used in conjunction with the 1-DoF force adaptive instrument from Latt *et al.* [7] to automatically generate large-area spiral mosaics. The quality, however, of the mosaics was limited as the instrument could only adapt in axial forces. Alternative to the active approaches, passive contact mechanisms were introduced. Giataganas *et al.* [9] developed a 1-DoF pick-up probe that can compensate for surface irregularities in robotic-assisted surgery using a pneumatic-based mechanism as an air bearing. Zuo *et al.* [10] employed a spring-based mechanism in the tip of a micro-scanning instrument and enhanced the stability further by integrating an inflatable outer balloon that stabilises the cavity structure under examination. These passive approaches demonstrated extended mosaicked areas but are limited in axial force compensation with non-linear spring-based mechanisms, while the use of balloon mechanism is limited to specific operations and dimensions. Another approach to generate local mm-scaled mosaics presented by Rosa *et al.* [11] incorporates a mechanical stabiliser on a micro-scanning tool to compensate for tissue motion and stabilise the surface under investigation. This simple and effective approach, however, increases the size of the instrument tip and is limited to local scanning since increased tissue deformation is introduced with the stabiliser. Finally, apart from bespoke instruments, the use of a large industrial robotic manipulator was explored by Rosa *et al.* [12] to build large area mosaics in flat 2D surfaces and study the tissue behaviour during endomicroscopic scanning.

In this work, a significant improvement over the aforementioned approaches is presented as a cooperatively controlled robotic manipulator. It showcases a 3-DoF force adaptive scheme that allows complex deformable 3D surfaces to be scanned and wide area mosaics to be generated. This robotic manipulator provides a stable mechatronically-enhanced platform for micro-scanning tools to acquire high resolution mosaics over 3D uneven moving surfaces.

II. MATERIALS AND METHODS

A. Hamlyn Arm

The Hamlyn Arm, presented in Fig. 1, is an articulated robot with 6 DoFs [13]. It is actuated by brushless DC motors coupled with harmonic drive gears. Each axis is controlled by an embedded motion controller EPOS2 by Maxon motor (Sachseln, Switzerland) which perform position, velocity, and current regulations. The arm weights 3.0 kg and reaches 780 mm in a straight configuration. The drive components are chosen so that the arm can manipulate a maximum payload of 1.5 kg with limited speed and acceleration. The joints can be backdriven by the operator in case of power loss. The arm communicates via a CANopen bus with the computer system in which the control system is implemented. The control software runs on a Linux operating system which performs several tasks including: motion generation, inverse kinematics, and force control. Cartesian and joint trajectories are generated using the Reflexxes Motion Libraries [14].

B. Endomicroscopy

The microscope used in conjunction with this platform is an in-house high-speed line scanning endomicroscopy system. It can be used to obtain high-resolution images of stained tissue *in situ* through a flexible fibre bundle (probe).

The endomicroscopy system generates optically-sectioned fluorescence microscopy images at 120 fps. It consists of a Cellvizio UHD probe (Mauna Kea Technologies, France), coupled to an in-house laser scanning and detector system, described fully in [15]. The probe contains a 30,000-core Fujikura fibre imaging bundle coupled to a distal micro-objective lens, providing a FoV of approximately 240 μm , a resolution of approximately 2.4 μm (based on Nyquist criteria) and a working distance of approximately 50 μm . It has 2.6 mm maximum diameter at the distal tip and it can be used in direct contact with the tissue surface.

The endomicroscopy probe is routed through a rigid tubular channel of a micro-scanning robotic tool and fixed proximally at the entry point. The channel allows other types of probes to be used as long as their diameter is smaller than 2.8 mm. The tool is mounted on a force sensor which is attached to the end-effector of the robotic arm. As a result, any force exerted at the tool tip is measured by the sensor. The demonstrated work can be used with any rigid instrument. Hence, the micro-scanning capability and further details of this tool are not presented in this work.

The imaging system is controlled via a dedicated software interface developed mainly in Labview (National Instruments, USA). Raw images are processed in real-time to remove the pixelation artefact (honeycomb pattern) from the fibre cores using a Gaussian filter. A background image subtraction is then performed to remove the fluorescence signal from the optical fibres. Real-time mosaic preview (of limited size) is generated by performing a simple pairwise registration of image frames using normalised cross-correlation (NCC), similar to [16], but is adapted to perform real-time mosaics at 120 fps. Further processing is performed to reduce the non-uniform light intensity between overlapping images using distance-weighted alpha blending. Videos are stored for post-processing to generate very large area mosaics using a similar approach.

C. Differential Inverse Kinematics

To manipulate the 6-DoF robotic arm, a Jacobian-based differential inverse kinematics is used. The standard iterative Newton-Raphson method is chosen to optimise the joint values such that the desired end-effector pose is reached [17].

In each iteration, joint values are computed using the damped least squares (DLS) inverse Jacobian ($\mathbf{J}^*$):

$$\mathbf{J}^* = \mathbf{V} \text{diag}(\hat{\sigma}_1^{-1}, \dots, \hat{\sigma}_n^{-1}) \mathbf{U}^T, \quad \mathbf{J}^* \in \mathbb{R}^{n \times 6}, \quad (1)$$

where $\mathbf{V}$, $\mathbf{U}$ are the right and left singular vectors obtained by a singular value decomposition (SVD) of the Jacobian, and $\hat{\sigma}_i^2$ are the i^{th} damped eigenvalues calculated as,

$$\hat{\sigma}_i = \begin{cases} \sigma_i & , \text{ if } \min_j (|\sigma_j|) \geq \sigma_{\min} \\ (\sigma_i^2 + \lambda_t^2) \sigma_i^{-1} & , \text{ else} \end{cases}, \quad (2)$$

and where

$$\lambda_t^2 = \lambda_{\max}^2 (1 - (\min(|\sigma_j|))^2 \sigma_{\min}^{-2}), \quad (3)$$

$i, j \in \{1, \dots, n\}$, and $n = 6$. For critically low singular values of the Jacobian, smaller than $\sigma_{\min}$, this approach provides damping to avoid high joint velocities. Otherwise, the damping is not applied when singular values are sufficiently large. This optimisation takes $\sim 10 \mu\text{s}$ per iteration to compute.

D. Workspace Analysis

The dexterity of the robot is depending on the placement of the scanning probe within the workspace of the robot. To ensure precise motion and a fast converging inverse kinematics, a probe placement within workspace volumes of high dexterity is desirable. The dexterity measure $\mathcal{D}$ is based on the manipulability measure:

$$\mathcal{M}(q) = \sqrt{|\mathbf{J}(q)\mathbf{J}(q)^T|}, \quad (4)$$

and augmented by the joint limit measure:

$$\mathcal{L}(q) = 1 - \exp \left\{ -\kappa \prod_{i=1}^n \frac{(q_i - q_{i,\min})(q_{i,\max} - q_i)}{(q_{i,\max} - q_{i,\min})^2} \right\}, \quad (5)$$

such that it is obtained as:

$$\mathcal{D}(q) = \mathcal{L}(q) \mathcal{M}(q), \quad (6)$$

and where $q_{i,\min}, q_{i,\max}$ are the lower and upper joint limits of the i^{th} joint respectively [18]. A workspace analysis, depicted in Fig. 2, was conducted to allow an optimum placement of the robotic system to the target anatomy.

The analysis is obtained by calculating the dexterity measure $\mathcal{D}$ for 10^{10} random robot configurations. In Fig. 2, each voxel of 6-millimetre edge represents the maximum dexterity of configurations whose end-effector position falls into it. The dexterity measure is not symmetric about the z -axis due to the limits of the base joint. Hence, the front-facing configurations have higher dexterity than rear-facing ones.

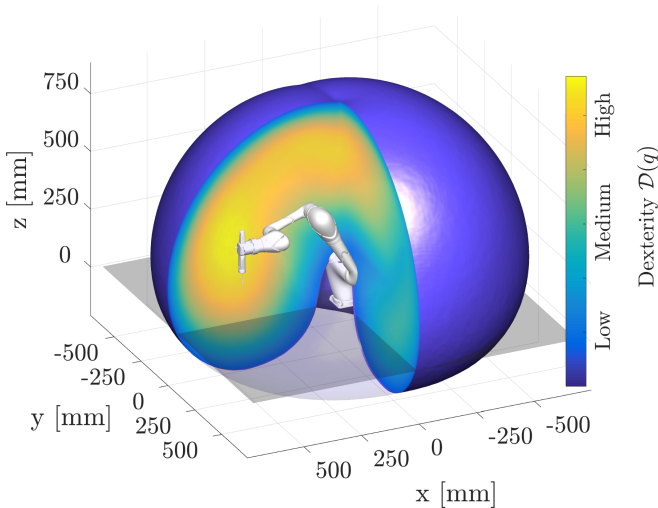


Fig. 2. Dexterity of the manipulator with the scanning probe within the reachable workspace calculated using the dexterity measure $\mathcal{D}$ in (6).

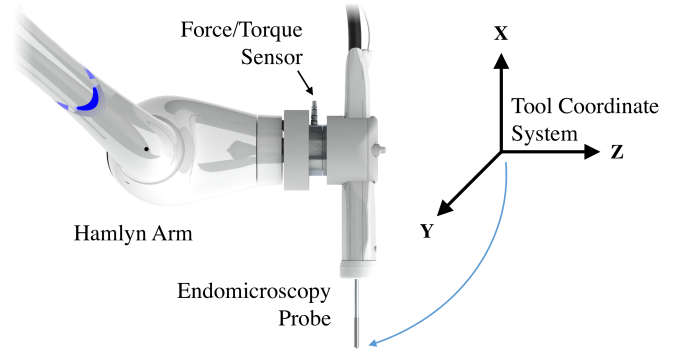


Fig. 3. Placement of the microscopy probe and the force/torque sensor at the end effector. A tool coordinate system is defined at the tip.

E. Contact Force and Orientation Control

The quality of microscopic image and the visibility of cellular structures are highly dependent on the probe-tissue contact force during image acquisition [19]. Maintenance of the probe orientation to be perpendicular to the contact surface can also drastically improve the image quality. For the robotic arm to be able to maintain the correct orientation with a steady contact force, a Mini40 force/torque sensor (ATI Industrial Automation, USA) is incorporated at the end effector. The sensor can measure torques as high as 1 Nm with 125 μNm of resolution and forces as high as 20 N with 5 mN of resolution, which is within the optimal range for endomicroscopy imaging [19]. The force/torque data is sampled and converted with a data acquisition PCI adapter (National Instrument, USA) running at 32 kHz sampling rate. The digitised data is then filtered with an IIR low-pass filter.

Fig. 3 presents the placement of the endomicroscopy probe and the force/torque sensor with respect to the Hamlyn Arm. The tool reference frame of the robot is defined at the tip of the imaging probe, where the x -axis is defined along the shaft of the probe. The z -axis is parallel to the normal of the end effector flange. During a scan, the probe automatically translates along the x -axis to establish a contact to the tissue. The orientation controller rotates the tool about the y, z axes. Translation in yz -plane is manually controlled by the operator according to the area of interest.

The contact force exerted axially on the shaft of the imaging probe is regulated by a closed-loop controller. This controller translates the imaging probe along the shaft in order to maintain the desired force. The block diagram

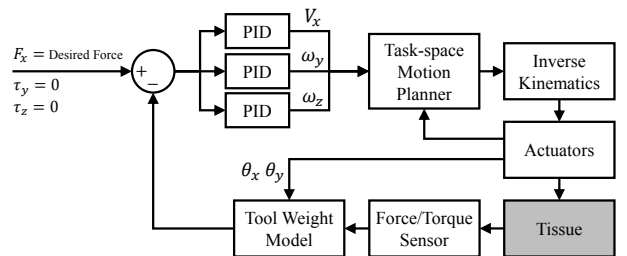


Fig. 4. Architecture of the 3-DoF force and orientation controller.

of the force controller is shown in Fig. 4. The contact force is measured and compared with the desired force. The difference is then fed into a PID controller through a clamp function, which limits the amount of this input to a predefined range to prevent large movements in events of contact with excessive force. The output of the PID controller is then used to set the translation velocity of the probe V_x .

The reference frame of the force/torque sensor is located at the middle of the microscopy probe and intersects with the x -axis of tool. When a perpendicular tool contact is established, the contact force that acts on the probe shaft is parallel to the shaft itself. Hence, there is no torque exerted at the reference point. However, when the probe orientation is not parallel to the surface normal, an amount of torques τ_x , τ_y , τ_z are exerted. Relying on these torque measurements, the orientation controller is implemented using two independent closed-loop controllers. The architecture of these controllers are similar to the contact force controller as shown in Fig. 4. The torque feedbacks τ_y and τ_z are used to set the angular velocities of the probe, ω_y and ω_z respectively. The torque setpoints for the orientation controller are zero in order to maintain perpendicular probe contact to the tissue surface.

F. Modelling and Calibration

With the placement of the force/torque sensor between the end effector and the microscopy probe, the sensor measures not only the contact force/torque, but also the weight of the tool itself. The tissue contact force required for microscopy is in the range of 50-100 mN. On the other hand, the weight of the tool is in a much larger range of 3-5 N. Before performing a scan, an initial bias value is applied to the force/torque acquisition system to subtract this amount of force. However, this bias value is dependent on the tool orientation since the probe's centre of mass is not at the reference point of the sensor. In order to get a useful contact force information to make the force control scheme effective, the variations of force and torque due to gravity are modelled and subtracted out from the measurements. Different cabling and attachment schemes can also affect the behaviour of this orientation-dependent offset. Based on these scenarios, a calibration method is implemented to model the baseline correction.

For the calibration, the tool is positioned in a dexterous region of the workspace with a sufficient clearance from the surrounding to eliminate external contact force. At this initial position, bias values are subtracted from the force/torque measurements. Then the tool is rotated arbitrarily along y and z axes about the tip while the force/torque data is recorded. The movement is performed throughout the available workspace of those two DoFs. Since this model is gravity dependent, the orientation parameters are defined as the angles of the tool with respect to the gravity vector. The robotic arm is assumed to be grounded. The orientation of the tool shaft (x -axis), θ_x and θ_y , correspond to the angle between the shaft and the gravity vector projected onto the xz - and yz -plane in the world coordinate system (Fig.2) respectively. In this setup, only the force and torques used for the closed-loop controllers are of interest for modelling.

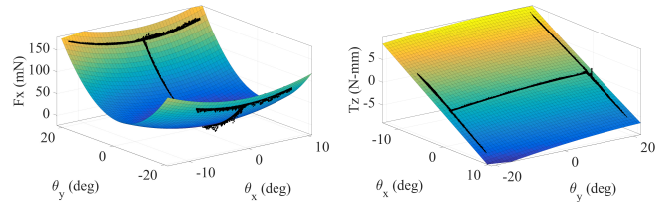


Fig. 5. Calibration of the probe offset weight in different sensor axes (F_x, τ_z) due to orientation changes. The black dots represent the measurement from the force/torque sensor. The fitted models are shown with coloured surfaces. The calibration for τ_y is similar to τ_z , hence is omitted.

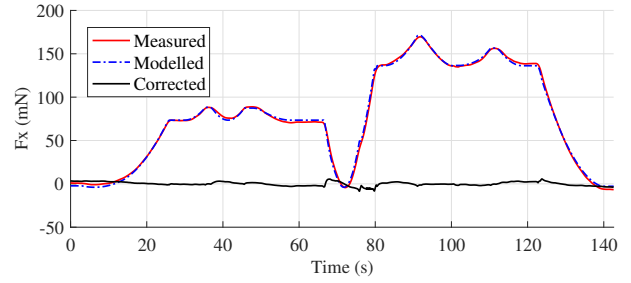


Fig. 6. Comparison of the measured force, modelled probe weight, and the corrected force F_x during orientation changes.

The gravity-related force F_x and torques τ_y, τ_z are defined as functions of θ_x, θ_y . The offset force/torque models are then generated from collected data using polynomial regression.

III. EXPERIMENTAL RESULTS

A. Microscopy Probe Weight Modelling

Each dimension of the collected data according to section II-F is fitted to a surface defined by a polynomial equation using regressions. From the experiment, F_x fits well with a second-degree polynomial, whereas τ_y, τ_z fit well with first-degree polynomials, which are shown in Fig. 5. The RMSE of the fits are 3.60 mN, 0.849 Nmm, and 0.256 Nmm respectively. The comparison before and after applying the correction model for F_x is shown in Fig. 6.

B. Force Controller

A bench test was performed with a silicone tissue phantom in order to evaluate the response of the force controller. In this experiment, the Hamlyn Arm with the micro-scanning tool performs a contact force control in a configuration similar to Fig. 2. The tool weight model is calibrated to eliminate the force offset due to the gravity. The force controller is then activated with varying setpoints from 50 to 500 mN. The step response of the force controller is shown in Fig. 7. This shows that the robotic system is capable of maintaining constant contact force to the tissue within a practical force range and be able to instantaneously change the amount of force as required.

C. Wide-area Microscopy Scanning

The robotic-assisted endomicroscopy system is tested on a porcine stomach tissue sample, shown in Fig. 8a. The task for this experiment is to complete a straight line scanning

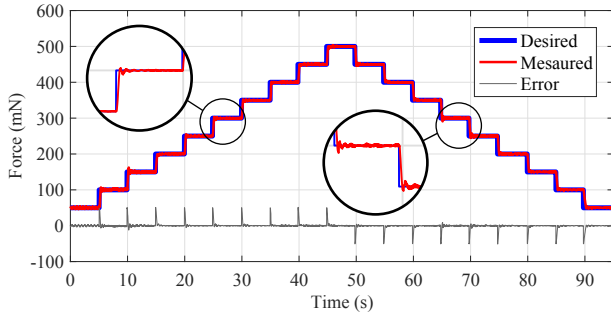
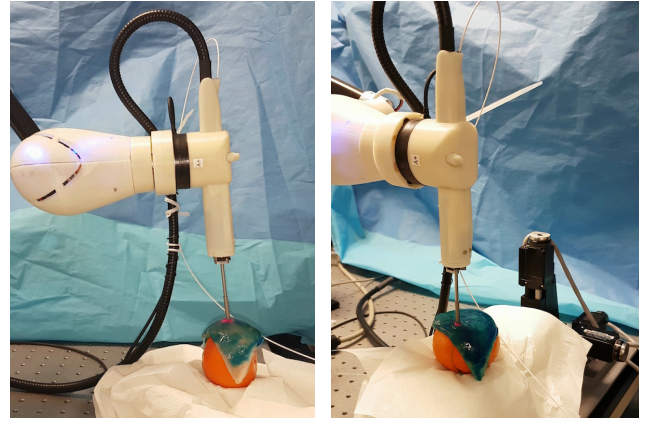


Fig. 7. Step response from the contact force controller on a tissue sample, showing the desired contact force, the measured force, and their difference.

on a spherical tissue surface. It is performed with 3 modes: A) 3D Contact Force and Orientation Control, B) 1D Force Control, and C) Manual Control. In the first mode, all the closed-loop controllers in Fig. 4 are used as the user moves the probe across the sample in xy -plane. In *Mode B*, only the contact force control is activated with a fixed vertical probe pose. Lastly, in the manual mode, the operator controls all 5-DoF movements ($x, y, z, \theta_y, \theta_z$) of the robotic arm. Since our aim is to obtain high quality images and also large area mosaics, the quality of mosaicking is selected to evaluate the performance of each experimental mode. Image quality can be derived not only using image criteria, such as entropy or blur metrics, but also using the NCC metric. The closer the NCC value is to 1, the better is the correlation between sequential images. It is a factor that gives an estimation for the quality of microscopic mosaics since these values are used as thresholds to discard low quality image pairs during mosaicking. The results of this comparison between control modes are presented in Fig. 9 in the form of histograms of the NCC values over a line scanning task. Also, the percentage of frame pairs that have NCC values more than 0.8 and 0.85 are calculated. As the speed is kept approximately the same in all trials, the overlap percentage is the same and therefore it has little effect on the comparison results.

As presented, *mode A*, where both the contact and the orientation of the tool are controlled, results in higher overall NCC value with a mean of 0.89. Also, 90.2% of the frame pairs have NCC values higher than 0.8. In comparison, *mode B*, where the probe orientation is fixed, the mean of the NCC value is 0.85 and the percentage of frames with NCC value greater than 0.8 is 80.8%. Finally, when the user has fully manual control of the robotic arm, the mean value of the NCC is 0.83 and approximately 75.2% of image pairs have NCC value greater than 0.8.

The generated image mosaics from the experiment are presented in Fig. 10. Due to size constraint, only parts of the overall mosaic images are presented here. As it is demonstrated, in accordance with Fig. 9, the mosaic image generated using both contact and orientation control presents better uniformity and enhanced contrast. However, the mosaic where the robotic arm is controlling only the contact presents distorted cell structure and blurriness in the



(a) stationary

(b) with a moving platform

Fig. 8. Experimental setups of the line scanning microscopy on a porcine tissue with a spherical surface.

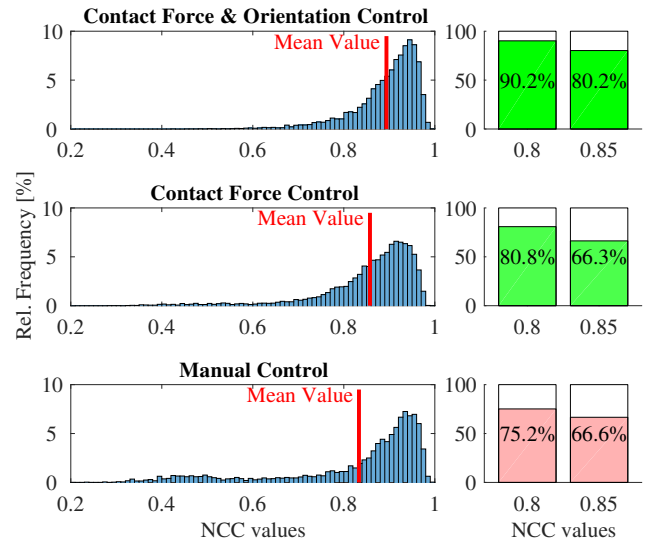


Fig. 9. Comparison of the NCC values from the mosaicking process between different control schemes applied during scanning.

beginning due to the lack of perpendicular orientation to the surface. This enhances the initial aim of this work that focuses on compensating not only for axial forces but the 3-DoF contact and orientation. Finally, the *Manual Control* mode generates non-uniform mosaics with non-consistent appearance as the operator failed to compensate for the 3D surface irregularities.

D. Motion Compensation

An experimental setup, as presented in Fig. 8b, is created to replicate the conditions encountered during *in vivo* examinations. The platform moves up and down repeatedly every 6 seconds with speeds of 1.00, 1.25, and 1.87 mm/s. Fig. 11 shows the performance of the force controller to track the movement while the desired contact force is set to 50 mN. The disturbance generated from the platform is compensated by the system with deviations of 8 mN at lower speeds and 15 mN at the highest speed.

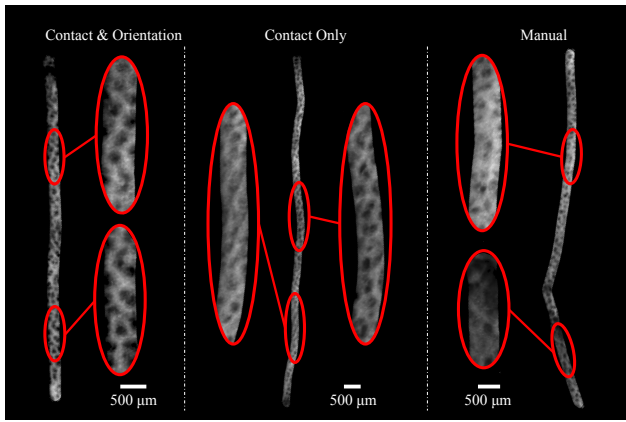


Fig. 10. Comparison of mosaicking results from endomicroscopy scanning with different control schemes.

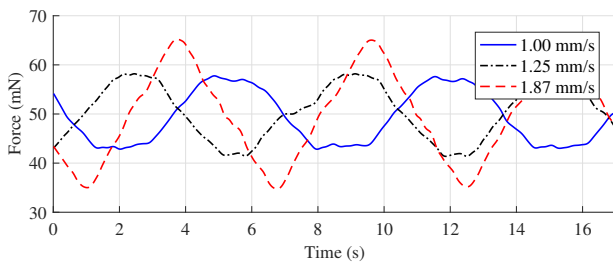


Fig. 11. Comparison of responses from the contact force controller on a moving tissue sample at different speeds. The setpoint is at 50 mN.

IV. CONCLUSIONS

This work presents a cooperatively controlled robotic manipulator with a 3-dimensional force control scheme. The system is equipped with a micro-scanning endomicroscopy probe allowing a wide area optical biopsy to be performed on an arbitrary tissue surface.

The robotic system automates the movement in 3 DoFs by three independent closed-loop controllers while the other 2-DoF translation is controlled by an operator to generate a scanning pattern according to the region of interests. An incorporated force/torque sensor provides high-resolution measurements for the feedback controllers. Compensation of the tool weight during orientation changes is modelled with a calibration, which allows accurate force control within ± 4 mN on average inside the dexterous workspace. Experimental results show that the image mosaicking with 3D force controller performs better than with only the 1D force controller or with fully manual operation.

Handling deforming, undulating surfaces during oncological surgery requires careful manual manipulation of imaging probes such as the pCLE and this adds burden to the operator and has been one of the limiting factors for routine clinical adoption of these new imaging technologies. The proposed scheme caters for both automatic contact force and orientation control and therefore is significantly simpler than existing robot assisted scanning schemes. This practically allows the operator to “point and scan”, allowing consistent large area surveillance via automatic image mosaicking. The

robotic arm used in this paper allows fully cooperative control and therefore can cover large anatomical regions whilst offering flexibility in robotic arm configuration. With increasing drive towards early and precision intervention in surgery, the proposed platform demonstrates an ideal synergy of human control and robotic assistance. This allows the surgeon to focus on operative tasks while imaging probes can assist seamlessly for detailed tissue characterization *in situ*, *in vivo*, without interrupting the normal surgical workflow, with autonomy but still under the command of the surgeon.

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