Chapter 3
Measuring the Mechanical Properties of Single Cells by AFM

Cell mechanics plays an important role in regulating cellular physiological activities. Cells within tissues are continuously exposed to mechanical cues including hydrostatic pressure, shear stress, compression force, tension force, and extracellular matrix stiffness [1, 2]. Cells dynamically respond to the stimulation of these mechanical cues by modifying their behaviors and remodeling their microenvironments [1]. This response is important in embryonic development as well as adult physiology, and is involved in many diseases, including atherosclerosis, hypertension, osteoporosis, muscular dystrophy, and cancer [3]. The interactions between cells and mechanical cues are often accompanied by the changes of cellular mechanical properties which have been shown to be effective biomarkers for indicating the pathological changes of cells [4]. For example, studies have found that red blood cells (RBCs) obtained from patients with malarial or sickle cell anemia are found to be stiffer and more viscous compared with healthy RBCs [5]. When normal cells become cancerous cells, the cellular elastic modulus significantly decreases: cancerous cells are more than 70% softer than benign cells [6]. The elasticity of cancerous cells is closely related to their metastatic ability: aggressive cancerous cells are softer than indolent cancerous cells [7, 8]. Hence detecting cell mechanics is attracting the attention of researchers for its potentials in complementing clinical medicine diagnosis. So far the diagnosis of cancer mainly relies on the morphological assay of biopsy cells, which is a very complex process, involving surgically removing tissue samples, staining and optical observation [9]. Besides, this method is not always 100% accurate because of the overlap between normal cells and cancerous cells on morphology at times. The detection of cellular mechanical properties can potentially be a useful complement to the traditional morphological assay. A study by Reich et al. [10] has shown that there were no significant differences in morphology between the diseased dermal fibroblasts from scleroderma patients and normal dermal fibroblasts from healthy donors, but diseased fibroblasts had reduced elastic constant than healthy fibroblasts, demonstrating the active role of detecting cellular mechanical properties in recognizing pathological cells. Plodinec et al. [11] have showed that there are significant
differences in stiffness maps between normal breast tissues, benign breast tissues and malignant breast tissues, confirming the indicative role of cell mechanics in cellular physiological processes.

### 3.1 Current Status of Measuring Cell Mechanics by AFM

AFM was initially utilized to measure the mechanical properties of biomaterials in the early 1990s [12–15]. In 1992, Tao et al. [13] measured the local Young’s modulus of cow tibia, and the experimental results proved that quantitative data on the mechanical properties of biomaterials can be obtained with unprecedented resolution by AFM. In 1995, Radmacher et al. [14] measured the Young’s modulus of mica coated with gelatin films in different liquids (including water, propanol, and mixtures of the two liquids), showing that the measured Young’s modulus of gelatin varied from 20 kPa to 0.1 GPa depending on the ratio of propanol to water. In 1991, Maivald et al. [15] simultaneously obtained the height image and stiffness image of the carbon fibre and epoxy composite by AFM force modulation technology and the results revealed the mechanical variations between the two materials, showing the potential of AFM in directly investigating the relationships between structural and mechanical properties of biomaterials. Since the mid-1990s, researchers began to utilize AFM indentation technique to measure the mechanical properties of living cells [16, 17]. In 1994, Hoh et al. [16] investigated the morphology and mechanical properties of Madin-Darby canine kidney (MDCK) cells, showing that the spring constant of MDCK cells was about 0.002 N/m. In 1996, Radmacher et al. [17] quantified the Young’s modulus of human platelets by adhering them to the glass substrate and the results showed that the Young’s modulus of human platelets were in the range of 1–50 kPa. With AFM indentation technique, we can monitor the dynamics of cell mechanics either by adding chemical molecules that can alter the cells or activate particular cellular biological activities. In 2000, Rotsch et al. [18] monitored the real-time changes of cellular Young’s modulus after the addition of drugs and the results showed that the disaggregation of cytoskeleton proteins can cause the significant changes of cellular Young’s modulus. In 2009, Cuerrier et al. [19] monitored the changes of Young’s modulus of human umbilical vein endothelial cells (HUVEC) after the stimulation of thrombin and bradykinin, showing that the two physiological agonists can make HUVEC stiffen. By combining AFM with confocal microscopy, in 2009, Pelling et al. [20] investigated the mechanical dynamics of single fibroblasts during early apoptosis. In 2009, Hu et al. [21] measured the Young’s modulus of lymphocytes in different states (using drug molecules to control cell states) and found that activated lymphocytes (∼20 kPa) had a larger Young’s modulus than resting and apoptosis lymphocytes (5–11 kPa). In 2012, Liu et al. [22] quantified the drug-induced mechanical changes of single living cardiomyocytes and found that the contraction force of cardiomyocytes significantly decreased after the stimulation of ibutilide.
The above studies were performed with conventional AFM tips (conical tip). Conical tip is sharp and measures the mechanical properties of cellular local areas, which facilitates us to correlate cellular mechanics with cellular structures (such as cytoskeleton) by simultaneously imaging and measuring cells. However, linking a microsphere to the AFM cantilever to measure cell mechanics can better characterize the mechanics of the whole cell. Using spherical tip to measure the cellular mechanical properties began in the early 2000s. In 2000, Mahaffy et al. [23] measured the Young’s modulus of 3T3 fibroblasts (1–3 kPa) by gluing a polystyrene bead to the cantilever. In 2005, Berdyyeva et al. [24] measured the mechanical properties of old and young human epithelial cells using spherical tip (silica bead with 5 µm diameter), showing that the Young’s modulus of older cells was 2–4 times larger than younger cells. In 2006, Leporatti et al. [25] measured the mechanics of resting and activated macrophages (lipopolysaccharide-stimulated), indicating that the Young’s modulus of macrophages decreased from 1.5 ± 1.1 kPa to 0.51 ± 0.31 kPa after the activation. In 2009, Oberleithner et al. [26] investigated the influence of potassium on the stiffness of endothelium cells using spherical tip (10 µm diameter) bead and found that the increase of potassium can soften the endothelial cells. In 2010, Lulevich et al. [27] found that keratinocytes were 6–70 times stiffer than other cell types (e.g., white blood cell, breast epithelial, fibroblast, or neuronal cells) using 40 µm diameter spherical tip. In 2011, Nikkhah et al. [28] used spherical tip to investigate the influence of growth medium on cell mechanics, showing that the reduction of serum in the culture medium can result in the decrease of cellular Young’s modulus.

3.2 Principle and Methods of Measuring Cell Mechanics by AFM

The principle of measuring cell mechanics by AFM indenting technology is shown in Fig. 3.1. Cells are immobilized on a substrate (for cell immobilization methods, readers are referred to Chap. 2). The mechanical properties (e.g., Young’s modulus) of cells are measured by obtaining force curves on the cells using conical tip (Fig. 3.1a) or spherical tip (Fig. 3.1b). Figure 3.2 shows the optical and SEM images of conical tip and spherical tip. At the force ramp mode, the AFM probe is controlled to perform approach-retract movement in the vertical direction on the cell surface. The deflection of cantilever is detected by a beam of laser via a four-quadrant photodiode position sensitivity detector (PSD) and the vertical distance between probe and substrate is acquired from the positional changes of piezoelectric ceramic driver. Figure 3.1c shows a typical force curve obtained on living cells, which reflects the approach-retract movement of AFM probe. For obtaining a force curve, the AFM probe firstly approaches and touches the cell. Before touching the cell, the deflection of cantilever is constant and the force curve is straight (denoted by the I in Fig. 3.1c). After the tip indents the cell, the deflection...
of cantilever changes and the force curve becomes bent (denoted by the II in Fig. 3.1c). When the loading force of the cantilever reaches the preset value, the tip retracts from the cell (denoted by the III in Fig. 3.1c). The retract curve becomes straight when the tip is separated from the cell (denoted by the IV in Fig. 3.1c). Cellular Young’s modulus can be obtained from both approach curve and retract curve depending on the theoretical models applied [29], while the retract curve can also be used for analyzing the adhesion forces [30].

There are many models for extracting the cellular Young’s modulus from the AFM-obtained approach curve, mainly including Hertz-Sneddon, Johnson-Kendall-Roberts (JKR), Derjaguin-Muller-Toporov (DMT), and Oliver-Pharr. Hertz model is applicable to spherical tip, while Sneddon extended it to conical tip [31]. Hertz-Sneddon model does not consider electrostatic forces, adhesion or friction between contact surfaces [32]. Hence, Hertz-Sneddon theory can only be applied
when the adhesion force is much smaller than the maximum load \[33\]. JKR model considers the adhesion forces inside the contact area whereas DMT model considers the forces outside the contact area \[34\]. Hence, JKR model can be applied in the case of large tips and soft samples with a large adhesion, and DMT model is applicable in the case of small tips and stiff samples with a small adhesion. Oliver-Pharr model considers the elastic response in the presence of plastic deformations to be the same as in the case of purely elastic deformation and also does not take into account the probe-sample adhesion. In practice, however, Hertz-Sneddon model is the most widely used model \[32\]. Hertz-Sneddon model is based on several assumptions that the sample being indented is homogeneous, isotropic, and infinitely thick \[31\]. It is obvious that these assumptions are not truly met in the case of indenting cells (cells are highly heterogeneous and anisotropic with a finite thickness). Nevertheless, studies have shown that when the indentation depth is less than 10% of the cell thickness, Hertz-Sneddon model is applicable \[35\]. When the indentation depth is larger than 10% of the cell thickness, then the AFM tip will feel the underlying substrate, which will make cells appear stiffer than they really are. In order to avoid the influence of substrate, Gavara et al. \[36\] integrated a correction factor into Hertz-Sneddon model and the results showed that the corrected model can effectively eliminate the substrate effects for thin samples (such as the peripheral areas of adherent cells). However, this method \[36\] requires the sample thickness which is obtained independently, increasing the complexity of this method.

By converting an approach curve into an indentation curve (Fig. 3.1d) according to the contact point (the indentation is obtained by subtracting the cantilever deflection from the vertical displacement of the probe), the Young’s modulus is extracted by applying Hertz-Sneddon model on the indentation curve. In most cases, the contact point is visually determined by manual \[37\]. The formulae of Hertz-Sneddon model are:

![Fig. 3.2 Optical and SEM images (insets) of AFM tips (a) Conical tip. (b) Spherical tip](image-url)
\[ F_{\text{cone}} = \frac{2E\delta^2 \tan \theta}{\pi} \quad (1) \]
\[ F_{\text{sphere}} = \frac{4ER^{0.5} \delta^{1.5}}{3} \quad (2) \]
\[ \frac{1}{E} = \frac{1 - v_{\text{tip}}^2}{E_{\text{tip}}} + \frac{1 - v_{\text{cell}}^2}{E_{\text{cell}}} \quad (3) \]
\[ \frac{1}{R} = \frac{1}{R_{\text{tip}}} + \frac{1}{R_{\text{cell}}} \quad (4) \]

where \( v_{\text{tip}} \) and \( v_{\text{cell}} \) are the Poisson ratio of tip and cell respectively, \( F \) is the loading force of tip, \( \delta \) is the indentation depth, \( E \) is the effective Young’s modulus, \( E_{\text{tip}} \) is the Young’s modulus of tip, \( E_{\text{cell}} \) is the Young’s modulus of cell, \( \theta \) is the half-opening angle of the tip, \( R \) is the effective radius, \( R_{\text{tip}} \) is the radius of tip, \( R_{\text{cell}} \) is the radius of cell. Because the Young’s modulus of living cells is much less than that of tip \( (E_{\text{cell}} < < E_{\text{tip}}) \), we can rewrite the formula (3) to:

\[ \frac{1}{E} = \frac{1 - v_{\text{cell}}^2}{E_{\text{cell}}} \quad (5) \]

Then the formula (1) and (2) can be rewritten as:

\[ F_{\text{cone}} = \frac{2E_{\text{cell}}\delta^2 \tan \theta}{\pi \left(1 - v_{\text{cell}}^2\right)} \quad (6) \]
\[ F_{\text{sphere}} = \frac{4E_{\text{cell}}R^{0.5} \delta^{1.5}}{3 \left(1 - v_{\text{cell}}^2\right)} \quad (7) \]

Living cells are often considered as incompressible materials, and thus the \( v_{\text{cell}} \) is 0.5. According to the Hooke’s law:

\[ F = kx \quad (8) \]

where \( k \) is the spring constant of the cantilever, the loading force \( F \) can be calculated from the cantilever deflection \( x \). After obtaining the loading force \( F \) and the indentation depth \( \delta \), the cellular Young’s modulus \( E_{\text{cell}} \) can be calculated according to the formula (6) and (7). The remaining parameters involved in (6), (7) are known or can be acquired by experimental measurement. The half-opening angle can be obtained from manufacturer or measured by SEM, and the spring constant of cantilever can be exactly calibrated by thermal noise method.
During the indenting process, the AFM tip firstly encounters the glycocalix, then the cytomembrane, and then either the intracellular organelles or the cytoskeleton [38]. For eukaryotic cells, the glycocalix and cytomembrane are very soft and can be neglected in AFM experiments [38]. Cell cytoskeleton is the main factor determining the Young’s modulus extracted from the force curves obtained on living eukaryotic cells [39]. In practice, in order to obtain the results with statistical significance, thousands of force curves are often recorded on many cells [34]. For each force curve, a Young’s modulus is extracted by applying Hertz-Sneddon model to fit the corresponding indentation curve. Then many Young’s modulus values are acquired and distribution of these Young’s modulus values is often fitted with Gaussian function (for symmetric histograms) or lognormal distribution (for non-symmetric histograms) [40]. The mean value and standard deviation are acquired from the normal/log-normal distribution fitting, which statistically quantify the different mechanical properties of cells. For example, not only tumor cells have a much smaller mean value of Young’s modulus than that of benign mesothelial cells, but also tumor cells display a narrow, spiked peak with little spread, whereas benign mesothelial cells display a broad peak [6].

3.3 Fabrication of AFM Spherical Tip

The spherical probe was fabricated by gluing a sphere to the cantilever of an AFM probe based on AFM micromanipulation [41]. The detailed process of spherical probe preparation is as follows (Fig. 3.3). (1) An AFM probe was mounted onto the head of AFM and the laser signal reflected off the probe cantilever was adjusted. (2) A drop of the polystyrene sphere solution (the diameter of sphere was \( \approx 20 \mu m \)) was placed on a fresh glass slide and a drop of two-part epoxy adhesive (Araldite adhesive) was placed on another position of the same glass slide by using a toothpick. (3) Under the guidance of optical microscopy, the AFM cantilever was moved to contact the epoxy adhesive and then retracted immediately. (4) The AFM cantilever was moved to contact a single sphere for 10 s and then retracted. After step (4), if the target sphere disappears from the glass slide, then the micromanipulation is successful, else repeating steps (2–4) are needed. Figure 3.3a is the optical image of AFM micromanipulations for gluing spheres and Fig. 3.3b is the optical image of spheres. The prepared spherical probes are placed in a probe box (Bruker, Santa Barbara, CA, USA) for 24 h at room temperature for the hardening of epoxy adhesive. The fabricates spherical probes were imaged by optical microscopy and SEM. Figure 3.3c, d are the optical top view image and SEM side view image of a microsphere glued to a tipless cantilever. With the method, microspheres can also be glued to conventional AFM probe with conical tip, as shown in Fig. 3.3e, f.
3.4 Measuring the Mechanics of Cancerous Cells with Different Invasive Abilities

With the use of the fabricated spherical tips, the Young’s modulus of four types of suspended cells was measured, including RBC, lymphoma Raji cell line, lymphoma Hut cell line, and leukemia K562 cell line. RBCs from healthy volunteers were diluted in phosphate buffered saline (PBS) and harvested by centrifugation for 10 min at 2000 rpm. Raji/Hut/K562 cells were cultured at 37 °C (5% CO₂) in RPMI-1640 containing 10% fetal bovine serum for 24 h before experiments. For AFM imaging, cells were dropped onto poly-L-lysine-coated glass slides and chemically fixed for 30 min by 4% paraformaldehyde. The glass slide was then washed for three times by Milli-Q ultrapure water (18.2 MΩ cm) and dried with a stream of nitrogen. For AFM mechanical measurements, living cells were dropped onto poly-L-lysine-coated glass slides. After one min, the glass slides were placed in a Petri dish containing Hank’s balanced salt solution (HBSS).

AFM cell imaging experiments were performed in air using a conventional probe (MLCT, Veeco Company, Santa Barbara, CA, USA) at contact mode with a scan rate of 1 Hz. The scan line was 256 and the sampling point for each scan line was also 256. Force curves were obtained at a constant loading rate and the sampling point for each force curve was 512. The cantilever deflection sensitivity was calibrated on the bare area of the glass slide and then the thermal tune adapter (Veeco Company, Santa Barbara, CA, USA) was utilized to calibrate the spring constant of the cantilever. Five cells of each type (RBCs, Raji, Hut, K562) were selected for measurements and 50 force curves were obtained on each cell. Cell Young’s modulus was extracted by fitting the force curves with Hertz-Sneddon model.
Figure 3.4 are AFM images of RBC, Raji, Hut, and K562 cells. Figure 3.4a, e are AFM height image and deflection image of a RBC respectively. The scan size was 12 μm. The unique bi-concave disk shape can be clearly seen. The section profile (Fig. 3.4 i) indicates that the diameter of the RBC was 7.5 μm. Figure 3.4b, f are AFM images of a Raji cell. The scan size was 40 μm. We can see that Raji cell was plump and circular. The line profile (Fig. 3.4j) reveals that the diameter of the cell is 25 μm. Mature RBCs do not have nuclei and are bio-concave disks, whereas Raji cells have nuclei and exhibit plump shapes. Hut cells and K562 cells are T lymphocytes and neutrophils respectively, both of which have cell nuclei. From the AFM images we can see that both of Hut (Fig. 3.4c, g) and K562 cells (Fig. 3.4d, h) are also circular and plump. From the line profiles, it can be seen that the diameter of the Hut cell is 16 μm (Fig. 3.4k), while the diameter of K562 cell is 28 μm (Fig. 3.4l). The RBC is clearly smaller than the three cancerous cells. The normal diameters of healthy human RBCs are 7.5–8.5 μm, whereas the normal diameters of lymphocytes and neutrophils are 6–20 μm and 10–12 μm respectively [8]. We can see that here the RBC diameter measured in Fig. 3.4 is in the normal range. The diameter of the Hut cell measured in Fig. 3.4 is also in the normal range. However, the Raji and K562 cells are significantly larger than their normal counterparts. This may because that the RBCs used here were from healthy volunteers, while Raji and K562 are cancerous cells which are often larger than healthy cells.

Figure 3.5 shows the process of measuring the Young’s modulus of RBCs by AFM. Figure 3.5a is a typical force curve recorded on living RBC. The force curve
includes an approach curve (black) and a retract curve (red). There is a gap (hysteresis) between approach curve and retract curve, which is caused by cellular viscosity. Cell is viscoelastic, possessing a viscosity of fluids and an elasticity of solids [33]. Besides, the gap is small (the gap between approach curve and retract curve recorded on the other three types of cells was significantly larger than that on RBC), indicating that during the approach-retract process, the viscosity of the RBC

Fig. 3.5 Process of measuring the Young’s modulus of RBC by AFM [8]. a A typical force curve recorded on living RBCs. b Approach curve in (a). c Histogram of the Young’s modulus extracted from the approach curve (b) and Gaussian fiting. d Contrast of experimental indentation curve and theoretical indentation curve. e Histogram of the Young’s modulus extracted from many force curves recorded on a cell and Gaussian fit. f Histogram of the Young’s modulus of five RBCs
was small and the elasticity was dominant. This is a consistent characteristic of RBCs since they have high elasticity. Biomembrane force probe technology is based on the use of the high elasticity of RBC [42]. The approach curve was converted into an indentation curve according to the contact point (Fig. 3.5b) and then the 500 nm range of the indentation curve was used to compute Young’s modulus. For each force curve, there were hundreds of discrete data points and each data point can be used to calculate a Young’s modulus. Therefore, many values of Young’s modulus were computed from an indentation curve, and a histogram was plotted (Fig. 3.5c). The histogram was well fitted by Gaussian fitting. Insertion of Gaussian fitted Young’s modulus (0.173 kPa) into the Hertz model formula produced a theoretical indentation curve that is compared with the experimental data in Fig. 3.5d. The good agreement indicates that the Hertz model is an adequate approximation of the sphere indentation process. For each RBC, 50 force curves were obtained and 50 values of Young’s modulus were computed; a histogram is shown in Fig. 3.5e. A Gaussian fit indicates that Young’s modulus of the RBC was 0.143 ± 0.059 kPa. Values of Young’s modulus for four other RBCs were 0.137 ± 0.06, 0.149 ± 0.1, 0.146 ± 0.027, and 0.143 ± 0.07 kPa. Figure 3.5f is the histogram of Young’s modulus of the five RBCs, showing that the Young’s modulus of RBCs was about 0.1–0.2 kPa.

By applying the procedure described above, the Young’s modulus of Raji, Hut, and K562 cells were measured and the results are shown in Fig. 3.6. We can see that the Young’s modulus of Raji, Hut, and K562 cells was 0.2–0.4 kPa, 1–1.4 kPa, and 0.6–0.7 kPa respectively. The Young’s modulus of Raji cells measured by conical tip was 150 ± 60 kPa [43, 44], which was significantly larger than the Young’s modulus of Raji cells measured by spherical tip (0.2–0.4 kPa) here. This may due to the different cellular structures probed by the tips. Spherical tip has a

![Fig. 3.6 Histogram of the Young’s modulus of RBC, Raji, Hut, K562 cells [8]](image-url)
larger contact area than conical tip. Conical tip primarily probes the cell cortex, whereas spherical tip probes both cortex and the underlying cytoplasm. Cell cortex is an actin-dense region of the cell lying immediately beneath the cell membrane [45]. Cell cortex is much stiffer than the underlying cellular structures (cytoskeleton and cytoplasm), resulting in that the Young’s modulus measured by conical tips is larger than that measured by spherical tips [34]. Previously, a study by Nikkhah et al. [28] has shown that the Young’s modulus of breast cancerous cells measured by spherical tip was 0.2–1.2 kPa, and Leporatti et al. [25] have shown that the Young’s modulus of macrophages was about 0.5 kPa. Here we can see that the Young’s modulus of RBCs, Raji, Hut, and K562 cells measured here with spherical tip are comparable to these results.

Comparing the Young’s modulus of these four types of cells, we can see that the order of increasing Young’s modulus is RBCs (smallest), Raji, K562, and Hut cells (largest). Mature RBCs do not have cell nuclei, whereas the other three types of cells have cell nuclei (as shown in Figs. 3.4, 3.7a), which may result in that RBCs are the softest among the four types of cells. The softness of an RBC makes it easy to deform, facilitating it to traverse narrow capillaries to carry oxygen to various parts of the body. Comparing the Young’s modulus of Raji and Hut cells, we can see that Hut cells are much stiffer. Raji cells are from Burkitt’s lymphoma that is an aggressive, malignant B-cell lymphoma characterized by a high degree proliferation [46]. The Hut cells are from Sezary syndrome, which is a cutaneous T-cell lymphoma characterized by indolent malignant cells [47]. We can see here that Raji cells are significantly softer than Hut cells. K562 cells are also from a type of indolent chronic myeloid leukemia cells [48], and we can see that K562 cells are significantly stiffer than Raji cells.

![Fig. 3.7](image)

Fig. 3.7 Cell mechanics and cancer metastasis [8]. a Structure of RBC, Raji, Hut, K562 cells. b Cancer metastasis process
As shown in Fig. 3.7b, in the process of cancer metastasis from a primary site to a distant site, cancerous cells must successively pass through the basement membrane, the extracellular matrix, and the blood vessel walls [49]. The cancerous cells survive the harsh conditions within blood vessels and squeeze out of them in distant sites. Jin et al. [50] investigated the mechanical properties of breast cancerous cells after treatment with bone morphogenetic protein (BMP) which promotes cell migration. The results showed that the cells became softer after BMP stimulation. Cross et al. [6] have shown that cancerous cells were much softer than normal cells. These results indicate that cell stiffness plays an important role in cell movement. Softness may make it easier for cancerous cells to cross various obstacles in the body. Hence it is reasonable that cancerous cells with different metastatic capabilities may have different stiffness. For the three cancerous cells investigated here, Raji cells are the most aggressive and the softest, while the Hut and K562 cells are indolent and stiffer, showing the close links between cell stiffness and cancerous cell metastasis abilities. Cellular mechanical properties are closely related to their structures, such as the cytoskeleton. The results here indicated that aggressive cancerous cells are softer than indolent cancerous cells, providing a mechanical insight into cancer metastasis. However, the underlying mechanisms that cause these differences are unknown and further researches (e.g., comparison of cytoskeletons between cancerous cells with different stiffness) are required.

3.5 Summary

(1) The procedure of measuring cellular Young’s modulus by AFM was established and AFM spherical tip was fabricated with the use of epoxy glue based on AFM micromanipulations.

(2) With the use of spherical tip, the Young’s modulus of RBCs and three types of cancerous cells with different invasive capabilities were measured, showing that aggressive cancerous cells were significantly softer than indolent cancerous cells.

References
